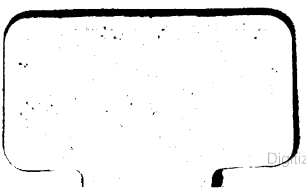
THE AUTOTOXICOSES

STERN



THE BOSTON
Medical and Surgical
JOURNAL.

Rec. May 15 1906.

Reviewed
Feb 1908

Book consists of two parts the first dealing mostly with various theoretical considerations concerning antitoxins and the second with their treatment. The author is familiar with the literature and conservative in his estimate of the value of observations made by the present biologic research. The section for therapeutics contains many reasonable suggestions, some of which are original with the author.

THE AUTOTOXICOSES

THEIR THEORY, PATHOLOGY AND TREATMENT

BY

HEINRICH STERN, Ph., M. D.

New York

PROFESSOR OF SPECIAL MEDICAL PATHOLOGY AND THERAPY IN THE COLLEGE OF PHYSICIANS AND SURGEONS, BOSTON; DIRECTOR OF THE INSTITUTE FOR MEDICAL DIAGNOSIS AND RESEARCH IN THE CITY OF NEW YORK; PHYSICIAN-IN-CHIEF, PHILANTHROPIN HOSPITAL IN THE CITY OF NEW YORK; PEDIATRIST AND PATHOLOGIST MISERICORDIA HOSPITAL AND THE HARTSDALE INFIRMARY; CONSULTING PHYSICIAN METROPOLITAN AND RED CROSS HOSPITALS; CHAIRMAN SECTION ON PHARMACOLOGY AMERICAN MEDICAL ASSOCIATION; PERMANENT MEMBER MEDICAL SOCIETY STATE OF NEW YORK; FELLOW OF THE NEW YORK ACADEMY OF MEDICINE ETC., ETC.

CHICAGO:
G. P. ENGELHARD & COMPANY
1906

To my brother
Arthur
this little book is affectionately
dedicated

PREFACE.

At no period in the history of medicine has hypothesis taken a more daring flight than just now. But what true progress in medicine has ever arisen on the flimsy structure of conjecture! Speculation, which is the alpha and omega of transcendental philosophy, should be limited and kept in check in the domain of science.

What else is the "autotoxic origin of disease" but unadulterated hypothesis in most instances? And yet, wherever one turns to, autointoxication is spoken of as something self-evident, and as of every-day occurrence. It has become a stock phrase with many.

The author of this little book is far from being a doubting Thomas. He conceives the probability that the animal organism can beget the etiological factors, the noxious material of its own ills. He knows, however, that a condition of autotoxicosis is very difficult to demonstrate as such, that it is not by far as common as is generally accepted, and that the great majority of disorders ascribed to self-poisoning are not at all of autotoxic origin.

In the following pages an attempt is made to define the status of the autotoxicoses and to arrive at an understanding, or if you wish, at a conception of the entire question involved. Physico-electric toxicity, first dwelt upon by the author, is discussed somewhat at length. A system of therapeutics evolved from toxicological principles and clinical experience comprises the second part of the monograph. Casuistry is limited to few illustrative instances. The appended brief glossary may be of help to the earnest reader. H. S.

New York, December, 1905.

CONTENTS

PART I

THEORETICAL, PATHOLOGICAL AND CRITICAL CONSIDERATIONS

CHAPTER I.

PAGE.

HISTORICAL EPITOME 15

CHAPTER II.

AUTINTOXICATIONS CONSIDERED IN GENERAL 18

CHAPTER III.

INTESTINAL AUTINTOXICATION 22

1. Entero-Toxicoses 22
2. Entero-Autotoxicosis 24
3. Autoprotection of the Organism against Enterogenous Poisons 31
4. The Chemical Protectors of the Organism 32
5. Food and Drug Idiosyncrasies and Autotoxemia 33
6. Symptomatology and Diagnosis of so-called Typical Cases of Entero-Autotoxicosis 36

CHAPTER IV.

INTESTINAL AUTINTOXICATION (CONTINUED) 39

7. Diseases and Complications whose Causes have been attributed to Intestinal Autintoxication 39

Dermatoses 40

Nervous and Mental Diseases..... 42
Periodical Vomiting..... 54
Asthma Dyspepticum..... 55
Tetany 56
Infantile Convulsions..... 58
Chlorosis 58
Pernicious Anemia and Leucemia..... 59
Cystinuria and Diaminuria..... 59
Intestinal Acetonuria and Diaceturia..... 60

CHAPTER V.

Catabolic Autintoxication..... 64
1. Definition and Scope..... 64
2. Histolytic Autotoxicoses 65
Autolysis 65
Acidosis 66
Autotoxicoses by Nucleolysis..... 72
3. Histoenzymic Autotoxicosis 76
4. Combined Retention-Histolytic Autotoxicosis..... 77

CHAPTER VI.

Critical Considerations of the Autintoxications..... 79
1. The Indefinite Use of the Terms "Autointoxication" and "Autotoxicosis"..... 79
The Biological and Chemical Methods for the Demonstration of Autintoxication..... 80

CHAPTER VII.

The Physico-Autotoxic State and the Pathogenesis of Uremia 88

CHAPTER VIII.

Recapitulation and Conclusions.....106

PART II

THERAPY OF THE AUTINTOXICATIONS

CHAPTER IX.

PAGE.

TREATMENT OF INTESTINAL AUTINTOXICATION.....113

1. General Considerations 113
2. Evacuation of the Gastro-Intestinal Canal.....115
3. Neutralization of Gastro-Intestinal Poisons.....120
4. Stimulation of Lymph Metabolism.....124
5. Augmentation and Acceleration of the Processes of Elimination 126

CHAPTER X.

TREATMENT OF INTESTINAL AUTINTOXICATION (CONTINUED)..128

Special Therapeutics 128

Dermatoses 129

Neuroses 131

Psychoses 135

Periodical Vomiting 137

Asthma Dyspepticum 137

Tetany 138

Infantile Convulsions 141

Chlorosis 142

Pernicious Anemia and Leucemia.....143

Cystinuria and Diaminuria..... 144

Intestinal Acetonuria and Diaceturia.....145

CHAPTER XI.

TREATMENT OF CATABOLIC AUTINTOXICATION.....147

1. Retention Autotoxicoses 147

2. Histolytic Autotoxicoses 149
Autolysis 149
Acidosis 150
The "Yolk Cure".....156

CHAPTER XII.

TREATMENT OF CATABOLIC AUTINTOXICATION (CONTINUED)...166
Nucleolytic Autotoxicoses 166
3. Histoenzymic Autotoxicoses 171
Graves' Disease 173
Myxedema 175
Pathological Adipositas 177
Addison's Disease 179
Acromegaly 180

CHAPTER XIII.

TREATMENT OF CATABOLIC AUTINTOXICATION (CONTINUED)...182
4. Combined Retention-Histolytic Autotoxicoses.....182
Cholemia 182
Uremia 188
Venepuncture 195
Puerperal Eclampsia 201

APPENDIX

Glossary 205
References 209
Index 214

Part I.

THEORETICAL, PATHOLOGICAL AND CRITICAL CONSIDERATIONS.

Chapter I.

HISTORICAL EPITOME.

Autochthonous intoxication as a factor in the aggravation or production of disease is by no means a conception of recent origin. The iatro-chemical school which flourished in the seventeenth century, numbering among its disciples men like Sylvius, Athanasius Kircher, Thomas Willis and Ettmueller, explained the origin of certain affections by putrefactive and fermentative changes in the blood; Sylvius, the founder of the chemiatric system, maintained that the health of an organism depended upon the relation of its fluids, which were acid or basic, but when united would occasion a neutral or less active compound, and that the causative factors of all diseases were either of an acid or alkaline nature. Marcus Marci, a physician of the same period, even after the discovery of the "vermiculi" in the blood and pus by Leeuwenhoek, Borelli, Petrus a Castro, Hagendorn and others, still contended that the production of vermiculi could ensue only in blood already in a state of impurity.

While endogenous causation of disease was thus anticipated two and a half centuries ago, investigations to clear this point were not undertaken until Bright's conception of uremia (1827-1840) as an autointoxic process. Charles Bouchard, however, was the first to systematically conduct such investigations on a large scale, and to him, who in 1887 published his now famous work, *"Leçons sur les autointoxications dans les maladies,"*

credit will always be due, not so much for the results which he obtained by his one-sided and often irrational experiments, but for the fact that he was the one to procure citizenship for the autointoxications in the vast field of clinical pathology, and to thus prepare the soil for further research.

Bouchard's work and views were soon taken up by his own countrymen, by many Italians and some English and American investigators. Medical literature from 1885 to 1897, especially that of the Latin countries, abounds in reports of biological experiments conducted in the sense of Bouchard and in treatises in which the etiology of many pathological states was considered and explained from the standpoint of autointoxication. Among a good deal of work of mediocre quality, much material of permanent value was furnished by Bouchard's followers, the most important of which will be found recorded in the following pages.

In Germany, on the other hand, where meanwhile bacteriology had taken almost exclusive possession of the domain of pathology, the theory of the autotoxic origin of disease has but slowly gained a foothold. The German pathologists, as a class, at this very day, to say the least, cannot be looked upon as its champions; reluctantly, and often in a limited sense only, have German clinicians from time to time admitted the possibility of an autochthonous toxicosis. This is the more astonishing as Senator, one of the foremost German internists, as far back as 1868 had denoted as "autoinfection" what Bouchard and v. Jaksch sixteen and seventeen years later comprised under the terms "autointoxication" and "autotoxicosis." For years the field had been cultivated dili-

gently by men like Petters (2), v. Voit (3), Schmiedeberg (4), Naunyn (5), and a host of others. It is indeed on the foundation laid, in the main, by German investigators upon which the superstructure, the autointoxic theory, has been erected.

Chapter II.

AUTINTOXICATIONS CONSIDERED IN GENERAL.

The term autointoxication implies self-poisoning of the organism by the retention of an excessive amount of normal products, or by the retention of abnormal products of its own digestive or metabolic processes. The autointoxication is said to be *intestinal* when its supposed causative factors have arisen within the digestive apparatus; it is *catabolic* when, apparently, it is intra— or intercellular in origin.

We are justified in speaking of intestinal autotoxicosis only in those instances in which the poisonous substances are of endogenous formation, that is, when they are truly intrabiontic. Preformed poisons, whether ingested as such or introduced into the organism by the medium of water or decayed food, as a matter of course, can never occasion autochthonous intoxication. The pathogenic microorganisms and their toxins, even if the latter have been produced within the intestinal tract, in the same sense, are ectogenous in character. Enteric fever, tuberculosis, diphtheria, cholera, tetanus, in short, the infectious diseases which may develop in any part of the digestive apparatus, are therefore not autointoxications. There is still a divergence of opinion as to the limitations of infection or autoinfection on the one hand, and autointoxication on the other.

v. Jaksch (6) classifies the diseases effected by the metabolic products of bacteria among the "Nosotoxi-

coses," one of his subdivisions of the endogenous intoxications. By the term "nosotoxicosis" he understands the toxic condition due to pathologic processes interfering with normal metabolism to the extent that products injurious to the organism are formed. Besides the diseases ascribed to bacterial products, he includes under this category all those abnormal states originating from spontaneous-autochthonous metabolic disturbances, as abnormal catalyses of hydrocarbons, carbohydrates and proteid substances. It is evident that the products of abnormal catabolism calling forth genuine autointoxication cannot be classified together with those due to the activity of ectogenous bacteria. A number of authors, with more or less modification, have accepted v. Jaksch's classification, and accordingly consider the bacterial poisons as true endogenous substances. Bouchard, too, (l. c.) does not differentiate between infection (autoinfection) and autointoxication—the infectious diseases in accordance with his view are autointoxications.

While the various manifestations in the course of infectious diseases are undoubtedly toxic in character, it is equally true that the poisonous material has been introduced as such, or has been produced within the body, by microorganisms coming from without. Bacterial products, as well as the toxic substances, yielded by food stuffs, cause toxicoses, but never autotoxicoses.

In a communication of comparatively recent date, Senator (7) terms all those intoxications "infection-autointoxications" that are occasioned by microparasitic toxins. In conformity with the opinion just expressed, the

toxicoses due to endogenous toxins of pathogenic bacteria should be designated as autoinfection.*

The question now arises, are there true intrabiontic intestinal poisons? This query may be best answered by another question: Do the cells of the gastro-intestinal mucosa participate in the production of toxic substances? To this, an affirmative answer may be given.

While intoxications arising in the intestinal tract in the great majority of instances are not autoxic in character, the anomalous processes classified together as catabolic autotoxicoses are of definite intra—or intercellular origin. The catabolic autointoxications may be subdivided into two great groups:—(1) those depending on retention of normal catabolic substances, and (2) those which are caused by products of retarded or perverted catabolism. To the first group are counted the pathologic manifestations due to the partial or complete retention of normal decomposition products and waste material accruing from cellular activity; that is, substances which normally are excreted by the kidney, lung, skin, intestines, salivary and lacteal glands. To the second group belong the autotoxicoses arising from perverted plas-

*Of course the subject of autoinfection is in itself a vast one. Besides the one just alluded to, there are various forms of autoinfection. The most common and indeed the most simple type of autoinfection is due to the passage of innocuous saprophytes of normal occurrence in certain parts of the digestive tract into other tissues and organs; for instance, the bacillus coli communis, ordinarily a harmless intestinal parasite, transmitted to the peritoneal cavity or the urinary tract, may give rise to fatal peritonitis or virulent pyelonephritis.

molytic and nucleolytic processes, and, probably, from anomalies of certain internal secretions.

In the following, the various types of autintoxication will be considered seriatim, thus:

I. INTESTINAL AUTINTOXICATION.
Absorption autotoxicoses.

II. CATABOLIC AUTINTOXICATION.
Simple retention autoxicoses. CO_2 poisoning.
Histolytic autoxicoses. Autolysis. Acidosis. Nucleolysis.
Histoenzymic autotoxicoses. Faulty "Internal Secretions.
Combined retention—histolytic autotoxicoses. Cholemia—uremia.

Chapter III.

INTESTINAL AUTINTOXICATION.

1. *Entero-Toxicoses.*—Fermentation and putrefaction are the two principal processes by which noxious substances are produced within the gastrointestinal tract. The fermentative products. usually the consequence of carbohydrate disintegration, as a general rule, are not as frequently factors in the causation of intestinal toxicoses as are the substances that immediately or indirectly result from putrefying proteids. These newly formed substances are not foreign to the digestive apparatus, they are practically of normal occurrence. In the healthy condition of the digestive organs, however, they are either excreted or transformed into innocuous compounds before they accumulate and display toxic qualities.

Among the enterogenous products of carbo-hydrate fermentation we find lactic ($C_3H_6O_3$), formic (CH_2O_2), acetic ($C_2H_4O_2$), proprionic ($C_3H_6O_2$), butyric ($C_4H_8O_2$), valeric ($C_5H_{10}O_2$) and succinic ($C_4H_6O_2$) acids. These acids are partly transformed into gases like CO_2, N, CH_4, and H; the remaining acids, neutralized by a fixed and volatile alkali which is derived from the putrefying proteids, are absorbed and undergo intrabiontic oxidation.

The principal putrefactive products of albumin occurring in the alimentary tract are, ammonia (NH_3), indol (C_8H_7N), skatol (C_9H_9N), phenylpropionic ($C_9H_{10}O_2$) and phenylacetic ($C_8H_8O_2$) acids, paraoxyphenylpropionic acid $C_9H_{10}O_3$), cresol (C_7H_8O), phenol (C_6H_6O), hydrosulphuric acid (H_2S), methylmercaptan (C

H_4S), most fatty acids as enumerated under the fermentative products of carbohydrates also caproic acid ($C_6H_{12}O_2$), acetone (C_3H_6O), leucin ($C_6H_{13}NO_2$), and tyrosin ($C_9H_{11}NO_3$).

Ammonia, under normal conditions, enters into combination and is absorbed; hydrosulphuric acid is eliminated as such in the gaseous form or is excreted as a sulphide; leucin and other amido-acids are absorbed; the aromatic substances enter into the blood, undergo various transformations and are excreted as ethereal sulphates.

It is the consensus of opinion among modern biochemists that all these products, like the very processes of fermentation and putrefaction, are the consequences of specific bacterial activity upon the ingesta.* The normal

*The intestinal bacteria may even play an important role in the process of nutrition. Max Schottelius (Ueber die Bedeutung der Darmbakterien fuer die Ernaehrung. Zeitschr. f. Diaet. u. Phys. Therapie, June, 1902.), observed that chicklings kept under strictly sterile conditions and fed on sterile food never grow heavier. Analogous to the seed of plants, their life continues at the expense of body material. None of his experiment chicklings lived longer than thirty days. Most perished after two weeks. Of course, these observations do not conclusively prove that animal development is dependent upon bacterial interference, but they tend to demonstrate that the factors producing sterility of and in the animal, call forth conditions which are averse to normal growth and development of the organisms.—Nuttall and Thierfelder's experiments upon newly born guinea-pigs (Zeitschr. f. physiolog. Chemie, Vols. 21, 22 and 23), on the other hand, evinced that such animals thrive for some time when no microorganisms are contained in any part of the alimentary tract. At any rate, the assistance of bacteria is essential in

intestinal microorganisms, however, are introduced with the foodstuffs. Inasmuch, therefore, as all these disintegration and decomposition products do not owe their existence to the cellular energy of the intestinal mucosa, the subject of enterogenous toxicosis, the latter a far more common occurrence than the genuine intestinal autotoxic process, must be eliminated from our further consideration.

2. *Entero-Autotoxicosis.*—As self-poisoning of the organism presupposes primary participation of its own cellular function, we must determine to what degree, if any, the intestinal mucosa, or its specific secretion, and the biliary fluid, are sources of toxic processes arising within the alimentary tract.

The rôle played by the bile in intestinal digestion is not yet fully determined. While some physiologists have considered it a mere excretion which does not participate in systemic processes, others have ascribed to it certain properties which it apparently does not possess. However, the bile is not an excretion, like the urine, for in that case it would not traverse the whole intestinal canal, and its principal components would normally not be reabsorbed in the intestines, nor does it, on the other hand, exhibit pronounced antiseptic qualities as it readily un-

the digestion of food containing cellulose. (Strasburger, Münch. med. Woch. 1903, No. 52.). According to the same author the normal intestinal bacteria are of importance to the human organism in other respects. They protect the small intestines from putrefaction and frequently prevent infection by pathogenic bacteria, which may have found access to the enteric canal. They also encourage peristalsis by the products of fermentation which they furnish from the carbohydrates.

dergoes putrefaction when removed from the organism.†

Bile is not a digestive secretion in the common acceptation of the term. In fasting animals, the amount of biliary secretion has been found but slightly diminished. It has been repeatedly demonstrated that in the presence of a permanent biliary fistula forming an exit for the bile, proteids and carbohydrates were completely digested, while a considerable quantity of the ingested hydrocarbons reappeared in the feces. This fact points to the participation of the bile in the absorption of fats. Moreover, it is also concerned in the splitting of fats into fatty acids and glycerin, and it assists in the process of emulsification, although it does not exhibit a specific fat-splitting enzyme.

Fatty acids which may occasion intestinal toxicosis are therefore not necessarily the result of bacterial activity. Their rapid and excessive production by the combined action of bile and pancreatic juice in the duodenum may lead to their accumulation and subsequently to an autointoxication. Again, the biliary-pancreatic secretions by an eventual perverted function may possibly give rise to anomalous products of fat disintegration and thus to an autochthonous intestinal toxicosis.

The intestinal mucosa and its secretion have not often been considered in connection with enterogenous auto-

†Wenhardt (Orvosi hetilap 1902, 2-6), investigating the antiseptic qualities of bile, found that the free biliary acids combined (1.2% glycocholic acid +0.6% taurocholic acid in the intestinal contents), even if they do not destroy the bact. coli communis, retard or diminish its multiplication. Cholic acid, glycin and taurin, in normal proportions, proved inactive in this respect.

intoxication. It seems plausible, however, that undue stimulation or disease of the intestinal mucosa causing anomalous secretion, either in quantity or composition, or in both; or that anomalous activity, or abnormal decomposition products of the enteric secretion may stand at the foundation of an autotoxic process.

That the mucosa of the small intestines of dogs or rabbits which were killed after twenty-four hours' fasting possesses toxic properties was proven by Druebert and Dehon (8). Its watery or glycerin extract is lethal in very small doses, if intravenously injected; the toxicity of the extract depends to some extent upon its coagulating activity.

The intestinal secretion is normally small in amount, particularly in the upper part of the bowel.* The pronounced alkaline character of the intestinal juice is due to sodium carbonate which may participate in fat emulsification. It contains neither a fat-splitting nor a proteolytic enzyme, but it exhibits enterokinase and certain amylolytic properties which latter are found mostly in the upper portion of the intestine. Erepsin, splitting hemialbumose, is another constituent of the intestinal secretion. The amylolytic enzyme is contained and exerts its function in the upper stratum of the intestinal mucosa rather than in its secretion. The various abnormalities in the enteric secretion may be the source of excessive amounts or of abnormal decomposition products.

*Hamburgher and Hekma (Jour. de Physiologie et de Pathologie générale, IV. 1902. Abst. in Biochem. Centralbl., 1, 1903) obtained through an intestinal fistula in a female patient from 50 to 125 Cc (in the mean 88 Cc) pro die of pure succus entericus which they examined for a period of 6 days.

One of the most potent factors of the intestinal secretion giving rise to the enterogenous formation of noxious substances seems to be the mucus. This occurs mostly in the large intestine, the bulk of whose secretion is composed of it. Normal intestinal mucus has not often been submitted to chemical analysis. Mucus excreted in the disease known as colica mucosa, irrespective of the form in which it appears, is always a pathological product and differs more or less from the normal product. The composition of normal intestinal mucus is very variable. The larger its physiological amount, the greater is its transparency and degree of alkalinity. Normally, the mucous secretion is at its height during intestinal digestion. It protects the mucosa by lubricating and surrounding undigestible material, and it assists in the elimination of various excrementitious substances. The mucus disintegrates readily, and most of its dissimilation products, as well as those of the gastric mucus are absorbed, much in the same manner as are the analogous substances of other glycoproteids. The most important constituents of the intestinal mucus are, of course, it mucins, of which, however, we know but very little. The longer the mucus remains in the intestinal canal, the more abundant will it be in fatty and proteid material, epithelium, leucocytes, mucous cells and other corpuscular bodies. A similar abundancy of formed elements in the mucus will occur in diseased conditions of the mucosa.

Mucus, not dissimilated in the normal manner and not egested with the feces, adheres to the intestinal wall, where it undergoes disintegration. While abnormal transformation of intestinal mucus frequently may be

of saprophytic or other microorganismic origin, it is certain that the dissociation may also ensue by autofermentation. The products of this autolytic process, especially when they occur in large amounts, may per se exhibit toxic properties. Directly or indirectly noxious substances, however, may result in various other ways, mainly from the catalytic action of mucus or its autolytic products, on the food-contents of the intestines.

The enteric secretion contains a substance considered a ferment by Pawlow, who has called it "enterokinase." While this possesses certain of the characteristics of a ferment, yet it does not seem to act like one in all respects: it combines quantitatively with fibrin without causing any alteration in the latter. According to Oppenheimer (9), a true amboceptor seems to be active in the enterokinase, as it combines with fibrin on the one hand, and on the other, like a complement, with trypsin. Hamburger and Hekma (1.c.) have determined that *enterokinase takes its origin in the secreting epithelia and that it is not produced by bacteria.*

The pancreas manufactures only the zymogen of trypsin, not the active ferment. The secretion of the small intestines exerts a specific stimulating influence upon the trypsinogen contained in the pancreas. While the unmixed juice from a pancreatic fistula exhibits very limited proteolytic qualities, it is at once rendered active by small amounts of fresh enteric juice. The activating principle of the enteric secretion is the enterokinase, or some other kinase not yet isolated.

Enterokinase, accordingly, is not an accidental substance, but an essential adjuvant in effecting trypsin activity. Its deficient secretion or its enforced latency by

an antikinase must result in insufficient trypsin formation and consequently in incomplete or anomalous proteolysis. It is even possible that the secernation may be entirely suppressed for the time being, or that it may be absorbed either as such or in an altered form. Again, in media too acid or too alkaline enterokinase loses its efficiency. Its activity is impaired after an exclusive and continued diet of carbohydrates resulting in hyperfermentation, that is in acid formation, as well as after a prolonged meat regimen ensuing in excessive putrefaction and strongly alkaline intestinal contents.

Deficient or perverse activity of any important enzyme, or of a complementary body like enterokinase, may occasion substances that will exert a greater or lesser degree of toxicity upon the organism. These substances may give rise to untoward phenomena similar to those called forth by some bacterial toxins.

Ever since the isolation of proteolytic ferments the question has been asked why they do not attack the walls of the gastrointestinal tract during life. The discovery of the "antibodies," and in this particular instance of the "antiferments," seemingly brings us nearer to the solution of this question.

In the extract and pressed juice of the carefully washed mucosa of the small intestines pronounced antipeptic and antitryptic activity was demonstrated by Weinland (10). The antiferment isolated from the pressed juice by precipitation and reprecipitation with alcohol is a decided retarding agent for fibrin digestion.*

*Other antiferments as for instance the antirennet obtained by Morgenroth (Centralbl, f. Bact. 26, 1899) in all likelihood have to fulfill similar offices in their respective domains.

The occurrence of normal amounts of antipepsin seems to regulate the peptic digestion, thereby preventing lesions to the gastric walls; the antitrypsin apparently performs a similar function for the small intestines. The perforating ulcer of the stomach, which in reality is not an ulcer at all but a round necrotic spot due to an autodigestion of a circumscribed area of the gastric organ, is probably the result of the deficiency or absence of antipepsin. The analogous morbid processes in the intestinal canal, the duodenal and follicular ulcers, are presumably the consequence of the nonoccurrence or inadequate production of antitrypsin.

Apart from the local lesions some of the subsequent constitutional symptoms may be attributable to the anomalous formation of the gastrointestinal antiferments. Furthermore, the local pathological process is a portal through which enteric poisons may gain entrance into the circulation. Continued nonproduction of the antiferments is in itself a source of autotoxicosis, as it favors the rapid absorption of the unmodified ferments, especially in the presence of a local lesion due to their absence; ferment action and toxic action, however, appear to be identical.**

In the foregoing, I have dwelt only upon a few of the

**The modified or inactive ferments, to a degree at least, are absorbed in the intestinal canal. Their modification or inactivity is due to the antiferments. Slowly entering into the circulation the modified ferment is innocuous; gaining access thereto when still endowed with fermentative powers, particularly when absorbed rapidly so that comparatively large amounts circulate in the blood at one time, it may behave like a toxic substance.

possible intrabiontic factors of intestinal autotoxicosis. It was neither my intention to elaborate on the facts mentioned, nor to exhaust the subject of the production of nonbacterial enterogenous poisons. For the present purpose, it suffices to know that many of these products may be of true intrabiontic formation, and that we are well justified in attempting to trace the origin of some disorders and of certain complications of disease to an intestinal autintoxication of some kind.

3. *The Autoprotection of the Organism Against Enterogenous Poisons.*—Normally the pernicious substances arising in the alimentary canal are either not absorbed at all or are transformed into harmless compounds before entering the circulation, or are soon attenuated or eliminated after they have passed into the blood current. The healthy organism is equipped to dispose of these products by various means, whether they are the result of normal or of pathological processes.

1. Some such substances—prior to absorption—leave the body in the gaseous form at the distal ends of the alimentary canal, others are excreted with the feces.
2. A number of intestinal poisons and the normal digestive ferments are converted into innocuous material, in which form they are transmitted to the circulation.
3. The normally functionating liver prevents from entering the general circulation or transforms into innocuous compounds such enterogenous toxic material which has traversed the intestinal mucosa and found its way into the portal circulation.
4. The antibodies circulating in the blood may cause attenuation or inactivity of the toxic matters conveyed to the blood.

The intestinal substances, accordingly, can enter the general circulation in those instances only in which there is insufficient or faulty activity of the hepatic organ. Moreover, if the supply of active antibodies is adequate, their transgression into the general circulation will not be followed by untoward phenomena. Their toxic activity is only displayed when they are allowed to accumulate in the blood, that is in such instances in which, besides impaired liver function and inadequate antibodies (either in amount or activity, or in both), there is insufficiency of either kidneys, lungs or skin, or of any two, or of all these organs.

The production of toxemia by enterogenous material is, in the majority of cases, the result of their incomplete conversion and subsequent cumulative action.

As long as the noxious substances are eliminated or destroyed in the ratio in which they are admitted into the blood current, toxic phenomena will not ensue. For these reasons, intestinal autotoxicosis is never an independent occurrence, but is always deuteropathic to an excretory or "internal secretory" disturbance.

4. *The Chemical Protectors of the Organism.*—Oxidation, reduction, hydration and dehydration are the protective reactions which are at the command of the organism to counterwork almost all known intoxications. "Addition" may be called a fifth protective reaction which may ensue in poisoning with certain substances. It is evident that the same defensive processes are displayed when the noxious material is of intrabiotic formation. However, as in the latter instance the nature of the poison is wholly unknown in well-nigh every case, the degree of participation of the various reactions in

maintaining the systemic equilibrium is beyond scientific demonstration.

The chemical protectors of the organism on which Fromm (11) some time ago has published a brief but authoritative brochure, are rather few in number. They comprise: blood alkali, albumin, hydrogen sulphide, sulphuric acid, glycocol, urea, cystein, cholic acids, glycuronic and acetic acids. Possibly a few more substances may be considered to act as protective agents, those enumerated, however, are all that are positively known to be such. All known protective agents are products of normal metabolism. They circulate in the organism either in the form and composition in which they are likely to be utilized, or in such condition that, if occasion arises, they are readily converted into reactive bodies. None of the protective chemical agents acts as a specific against a certain poison. The poisons rendered innocuous by albumin, hydrogen sulphide, sulphuric acid, glycocol, glycuronic acid and cholic acid are legion. The other protectors, urea, acetic acid and cystein, are each neutralizers of a number of body-poisons, of probably more, as Fromm (l. c.) suggests, than we are acquainted with at the present day. The neutralizing power of the chemical protectors for a large number of discrepant poisonous substances flatly contradicts the dominating bacteriological view according to which the protective agents which the organism produces to defend itself against the bacterial toxins are always or at least often specific neutralizers of specific toxins.

5. *Food and Drug Idiosyncracies and Autotoxemia.*— The clinical pictures of various autotoxic processes are often analogous to those which are the consequences of

habitual toxicoses occurring in some individuals after introduction of certain foodstuffs or drugs. The subsequent behavior of such material in the economy may not differ from that of autochthonous production. Both the substances yielded by ingested matter during the normal processes of fermentation and putrefaction, and those elaborated by and with the aid of normal cellular activity, are not in themselves poisonous to any degree, provided they are not directly carried into the circulation, or, if introduced therein, are soon eliminated or definitely neutralized. Intestinal autintoxication and alimentary toxicosis are in the last instance depending not so much on the admission to as on the retention in the blood of material, incompletely converted, normally innocuous or almost so.

Leaving out of consideration the manner in which the different substances gain entrance to the blood, we find that the various idiosyncracies (as well as dyscracies) are more or less the result of faulty elimination. This may be due to structural or functional disease of one or more of the emunctories, or to the affinity to combine with the invading substances exhibited by certain cells or groups of cells or by material circulating in the blood. The habitual occurrence, for instance, of skin affections like urticaria or erythema after ingestion of fish, strawberries, pickled foods, etc., is always due to the accumulation in the blood, or the subsequent fixation by cellular or other bodies, of certain of their disintegration products.

It is evident that a number of substances elaborated during digestion, when absorbed rapidly or in large amounts, tend to disturb the molecular constitution of one or more organs and of the body liquids to an unusual

degree and for a period beyond the physiological *norm.* The resistance offered by the organism against the disturbing elements varies in different individuals. In the absence of a disease or disorder of the emunctories the resistance is inversely proportionate to the amount of certain body constituents and their degree of affinity for the absorbed material; i. e., the greater the amount and affinity the smaller the degree of individual resistance. According to Lewin (12) there undoubtedly exists a personal toxic equation. And, there is also no doubt about the existence of an *individual autoxic equation.*

The idiosyncracies—the personal toxic equations and not the psychical aversions—for a number of remedies have always their physical or chemical substrata. The occurrence of iodism after administration of moderate doses of alkaline iodids frequently points to the existence of chronic interstitial nephritis, or advanced phthisis pulmonum. The iodids have a toxic effect in these diseases because, in the one case, they pass but slowly into the urinary secretion, and in the other, their exhalation by the lungs is more or less retarded. The administration in the usual manner of rheum in chronic parenchymatous nephritis is likewise apt to be followed by toxic phenomena; again, there is no doubt that tardy excretion of chrysophanic and rheumic acids, and calcium oxalate, substances introduced by the rheum, stands at the foundation of the toxemia.*

*Of course, the organic lesion as such may not be the direct cause of the retention of substances which are excreted normally. They may combine with certain elements in the organism which are the result of the local affection or concomitant therewith.

6. *Symptomatology and Diagnosis of so-called typical Cases of Entero-Autotoxicosis.*—Intestinal autotoxicosis—or what is considered such—is a not infrequent occurrence in the train of manifold acute or chronic disturbances. Its appearance is more or less paroxysmal, the individual attacks differing in severity and duration. When the underlying digestive disorder is of a chronic nature, the autotoxic phenomena may also assume an apparent chronicity. This, however, is not in reality the case. The attacks are always paroxysmal in character. However, in a succession of slight attacks, which may ensue in chronic conditions, the paroxysmal nature of the individual attack may not readily be discernible.

An enterogenous autotoxic process may exhibit the following train of symptoms:

DISTURBANCES OF THE ALIMENTARY TRACT: Eructation of gases, nausea or vomiting; bloated abdomen; intestinal colic; diarrhea or constipation.

NERVOUS AND MENTAL DISORDERS: General depression and languor; cephalalgia; vertigo and somnolence; syncope; irritability; amnesia; various motor and sensory disturbances.

Occasional symptoms.—

AFFECTIONS OF THE SKIN: Icterus; urticaria; acne; erythema, etc.

AFFECTIONS OF THE KIDNEYS: Oliguria; albuminuria; hyaline casts.

Other occasional symptoms: Chills; moderate temperature elevation; profuse perspiration; dyspnea.

Digestive and nervous disturbances are always present; their association furnishes the typical picture of any non-lethal toxicosis. The skin phenomenon most charac-

teristic of an intestinal autointoxication seems to be icterus, although it appears neither frequently nor in a very pronounced degree. Urticaria and other skin affections are the casual concomitants of any form of intestinal toxicosis. The presence of oliguria or albuminuria adds to the severity of the attack.

The syndrome of a case of intestinal autintoxication is in general analogous to what the French call "vertige de l'estomac." In this affection, however, the vertigo is not always the most prominent symptom, nor is its source confined to a gastric difficulty. Moreover, gastric vertigo is not always the direct expression of an autintoxication; occasionally it may be the result of reflex disturbances which may have arisen in consequence of a toxic process.

The differential diagnosis between enterogenous autotoxicosis and ectogenous toxicosis or infection, when the identity of the poison is not established and the analogy of the clinical pictures alone is considered, appears often impossible.

The diagnosis of an enterogenous autointoxication therefore is positive only in a comparatively small proportion of the cases. In differential diagnosis the following considerations should guide us:

a. *The occurrence of toxic phenomena in one individual only.*

In case the pathological condition is due to an infection by the medium of water, milk or meat, or to an ectogenous poison introduced by the food, or liberated by the latter in the intestinal canal, it stands to reason that the partaking of the same food by a number of persons may call forth similar toxic symptoms in more than one individual. While, under these conditions, the occurrence

of the aforementioned clinical picture in one individual only does not definitely stamp the instance as one of intestinal autointoxication, it precludes to a great measure the existence of an infection or an ectogenous intoxication.

b. *The occurrence of toxic phenomena after ingestion of taintless food.*

This point is virtually covered by the preceding one, excepting that the noningested portion of the food is submitted to the scrutinizing analysis which fails to demonstrate any poisonous qualities therein.

c. *The occurrence of toxic phenomena independent of the ingestion of food.*

The syndrome of a toxicosis appearing some time after assimilation of the last digested food, as in the morning, or during a prolonged period of abstention from nourishment and in the absence of a too exuberant flora of intestinal bacteria, must necessarily be the outcome of an intrabiontic process. However, the pathological state in this eventuality may be due to catabolic as well as to intestinal autointoxication.

The fact that the toxic symptoms vanish immediately after removal of the cause is thought by Ewald (13) and others to be characteristic of an enterogenous autointoxication. This, however, is plainly not the case, as similar amelioration or disappearance of the phenomenon is also noticed after extermination of the causes of any form of intestinal toxicosis. The course and abrupt cessation of Senator's well-known case of hydrothionemia (14) have repeatedly been mentioned in support of its autotoxic origin; however, whether this remarkable instance of H_2S poisoning was a simple toxicosis or an autotoxicosis, the pathological condition would have soon subsided after the elimination of the causative factors.

Chapter IV.

INTESTINAL AUTINTOXICATION (CONT'D).

7. *Diseases and Complications Whose Causes Have Been Attributed to Intestinal Autintoxication.*—While all the disturbances considered to be of enterogenous causation exhibit the autotoxic syndrome dwelt upon in the foregoing, or at least, are ushered in with it, yet it stands to reason that certain phenomena may attain a greater degree of prominence in the various instances. Accordingly, the origin of a number of apparently discrepant affections has been ascribed to autotoxic processes arising in the intestinal tract. In as far as the characteristic feature of each of these affections finds its prototype in the paroxysmal attack described before, and in as far as the latter has occurred or is still prevailing, these affections, clinically speaking, must be looked upon as expressions of toxicoses. In these cases the characteristic phenomena are the aggravation of the analogous symptoms of the uncomplicated attack. In other words, similar toxic processes may stand at the foundation of all the diseases of supposedly enterogenous causation, but in different individuals the poison may invade and impair the same organs in a different degree, or they may invade different organs altogether.

While it is undoubtedly true that checking the cause does not always repress the morbid effect, yet the specific clinical picture of an intestinal autotoxicosis cannot attain chronicity after the removal of its cause. The pathological substratum of a chronic form of intestinal

autointoxication enunciating itself in specific, *enduring* phenomena can hardly be conceived.[1] Such an autointoxication presupposes the uninterrupted production of a specific poison or poisons by a specific morbific procedure for each specific disease or complication, or of the continuous formation of specific enterogenous substances keeping certain organs or structures in a specific state of impairment, processes the occurrence of which will always remain more or less undemonstrable. However, as it is just as difficult to prove that the various diseases are *not* the consequence of enterogenous autointoxication, and as all of them (at least during some phase, or by complications) exhibit phenomena which we are forced to regard as expressions of toxic or autotoxic states, they will find due but brief discussion in the following:

DERMATOSES.

We have already seen that the condition of the skin may be symptomatic of more or less paroxysmal processes of autotoxicosis. The eventual chronicity of a toxic skin

---

[1]There is little doubt that certain substances may give rise to specific effects without causing local alterations, viz., alcohol, many alkaloids, glucosides, etc. The non-local activity is a characteristic of blood- and nerve-poisons (Albu). Their effect, however, is of a more or less transitory nature unless their *continued* use has brought about structural changes. These poisons, if not habitually employed, work paroxysmically, similarly as do those formed in the enteric canal. Cessation of the absorption of enteric poisons is followed by cessation of the toxic phenomena. These may not stop abruptly but they gradually decline in severity, so that after a comparative short period the normal condition of the organism is re-established.

affection does not necessarily mean that its underlying factor continues without interruption.[2] While it is true that there must be insufficiency of the excretory organs, including the skin, before autotoxic symptoms manifest themselves in the latter, it is equally true that excepting, perhaps, glucose in hyperglycemia and the resulting dermatoses, we have not isolated any intrabiontic chemical substance to whose occurrence a particular skin affection may be ascribed.

Nevertheless, Tommasoli (15) maintains that his "Keratodermites," among which he classifies the most dissimilar skin affections as lichen, psoriasis, ichthyosis, dermatitis exfoliativa, eczema chronicum, etc., are the result of toxic substances continuously produced in the organism and retained therein; the toxic products, he asserts, enter the circulation in all chronic maladies accompanied by nutritive and metabolic disorders, and may, at times, involve the skin.

Urticaria, erythema, acne, pemphigus and other affections belonging to this category may be the external manifestations of an acute toxic or autotoxic process. They usually disappear as suddenly as they have come forth. They endure, as a rule, not longer than their

[2]This fact is well illustrated by a case of Bernard and Gaucher. A man, 44 years of age, affected with toxic nephritis, exhibited *cutaneous manifestations at each attack of uremia.* At first, alopecia universalis, and subsequently vitiligo and prurigo supervened. As with the aid of the methylene-blue test, the renal permeability was found normal, the observers concluded that the toxemia was not due to renal inpermeability, but that the same toxic material was responsible for both, the nephritis as well as the cutaneous symptoms.

causative factor or any of the other toxic manifestations.

Knowing, therefore, that every autointoxication, including its eventual skin manifestation, is a process limited in duration, we fail to see how chronic eczema, for instance, which might last a lifetime, can be classified among the autotoxicoses. This would presuppose a continued poisonous state of the organism with manifold pathological phenomena other than the eczema. We know, however, that eczema concurs with such a grave condition only in the rarest of instances.

NERVOUS AND MENTAL DISEASES.

The nervous and mental manifestations of the typical autotoxic process originating in the enterium have been touched upon previously.

Besides these, there are a number of other nervous affections, seemingly disease-entities, that are by some supposed to arise from the basis of an autointoxication. The different types of neuralgia, neuroses, meningoform disturbances, acute ascending paralysis, periodic paralysis, myasthenia gravis pseudoparalytica and other nervous disturbances have been referred to, with more or less justification, as being autotoxic in origin. While this assumption seems rather far-fetched in the great majority of instances—intestinal autointoxication, theoretically speaking, may be an element in their production but not their only causative factor—the epileptic attack and kindred affections frequently appear so intimately related to typical cases of enterogenous autotoxicosis that we cannot refrain from considering some forms of epilepsy in the light of an autointoxication.[8]

[8] "A Case of Grave Intestinal Autointoxication," the clinical picture of which resembles that of meningitis, was reported

Narcolepsy, a sudden uncontrollable inclination to sleep, occurring repeatedly and after varying intervals, is looked upon by Furet (16) and Sainton (17) as a manifestation of autointoxication. Furet draws attention to the fact that seizures of pathological somnolence may occur in he course of nutritive disorders, such as diabetes mellitus and polysarcia; during the acute infectious diseases, such as influenza, enteric and typhus fevers; as a consequence of alcoholism or other intoxications, and as the result of drug narcotization. He believes further that epileptic attacks, which he with others also

---

by Stuertz (Berl. klin. Wochenschr. 1903. 23). The patient suffered from gastroenteritis and obstipation; bradycardia and high arterial tension were present; the urine contained very large amounts of indican. The grave brain symptoms at once disappeared after the administration of calomel, and through evacuation of the alimentary tract. This case, undoubtedly, was one of intestinal toxicosis, but the author has not demonstrated the genuine auto-toxic character.

There is, however, no other than the clinical proof that such an autotoxicosis is of intestinal origin. Recent experimental work concerning the causation of epileptic convulsions rather seems to point to certain *metabolic* disturbances as being their etiological factors. Mott and Halliburton (Lancet, April 13, 1901), and Donath (Zeitschr. f. physiol. Chemie, XXXIX, 526), for instance, have demonstrated that in epilepsy and some other affections of the nervous system the cerebrospinal fluid contained augmented quantities of cholin. (This is the only decomposition product of lecithin, which latter is the result of degenerative processes of and in the nerve fibers.) Injection of cholin into animals, made by Donath, called forth localized as well as general convulsions. Such convulsions did not occur after injection of NaCl solutions in various concentrations. He is of the opinion, thereore, that cholin may stand at the foundation of the epileptic convulsions.

considers a manifestation of intoxication, frequently are synchronous with narcolepsy.

The following detailed study of a classical instance of this condition which had been under my observation for some time (18) is given for four reasons:

a. To show how to proceed in the investigation of an affection of supposedly intestinal autotoxic origin.

b. To demonstrate the limitations of Bouchard's method for the recognition of autotoxic processes.

c. To evince our inability in establishing the dependence of a given clinical picture from the morphological and chemical findings.

d. To have a basis from which to proceed in a later chapter.

William S.; aged thirty-five; unmarried; native of Ireland; four years in United States; car conductor; was referred to me on April 30, 1901, for a supposed gastric disorder.

The family history does not evince any neuropathic traits. Patient is free from lues; is sexually disinclined; is a total abstainer from intoxicants and tobacco, and, with the exception of frequent attacks of gastric indigestion, that he now attributes to his former diet, in which farinaceous material greatly preponderated, enjoyed good health until about six years ago. Since that time he is afflicted with daily recurrences of hyperesthetic sensations on the forehead and eyebrows, and with sleeping seizures. For the last two years the daily attacks of somnolence have become more intense and of longer duration. In April and May of that year his sleepiness became so great that he was compelled to discontinue his work. Since then, under an exclusive milk regimen, and with

the assistance of various therapeutic measures, he is enabled to follow his occupation, although the intensity-degree of the diurnally recurring somnolence has hardly been diminished.

The sleeping seizures occur independently of the ingestion of food, as I have convinced myself by actual experiment, and inevitably set in between ten and eleven o'clock in the morning. The spells last till three or four in the afternoon; often the trancelike condition continues for the rest of the day. The patient will fall asleep, if disengaged, and only by the utmost sheer brutal will power is he able to resist an attack of sleepiness occurring during working hours. That is, he tries to withstand the irresistible desire to lie down and to sleep, by holding on to the railing or the straps of the car and making pitiful efforts to keep his eyelids apart, but notwithstanding his resistance he feels that virtually he is asleep; he knows that he is but semi-conscious, and that he performs his duties in an automatic way.

The patient's extreme morbid somnolence is best characterized by his own words: "Were I to fall into a pool during one of these attacks," he says, "I would be too tired to raise myself up, although I would be conscious enough to know that I might be drowned."

The patient possesses an active mind and is quick of perception. He is not a hysterical person in the sense that he is afflicted with minor phenomena of that affection. He is free from vertigo at all times. He never suffers from cephalalgia, but his head frequently feels full and heavy. He perspires profusely, especially on the hands, feet, and forehead at all times and irrespective

of the prevailing temperature, but particularly before the lethargic or narcoleptic condition sets in.

While the pathologic somnolence apparently does not influence the physical condition of the patient, his physiological sleep during the night does not seem to refresh him. For when he rises at 6 a. m. after eight or nine hours of sleep, he really feels more fatigued than he did on retiring the previous night. This languor is gradually subsiding toward eight o'clock, one and a half hours after breakfast.

The physical examination of thorax and abdomen revealed nothing unusual, except the fact of a weak, slightly hypertrophied heart and a tender, dilated stomach, extending to two centimeters from the umbilicus.

An analysis of the stomach contents, after a test breakfast consisting of 500 cc of weak tea and one dry roll, showed the following:

Gastric contents withdrawn one hour after ingestion of test breakfast: amount withdrawn, 240 cc; reaction, acid; hydrochloric acid; 0.36 per cent; lactic, acetic, and butyric acids, absent; pepsin, present; activity normal (fibrin dissolution); starch, unconverted in the unfiltered contents; erythrodextrin in filtered portion.

The microscopic examination revealed: starch granules, in various modifications, fat globules, epithelium, mucous corpuscles, yeast fungi, sarcinae ventriculi, and various nonpathogenic bacteria and micrococci. The stomach affection accordingly was diagnosed and treated as hyperchlorhydria, dilation and faulty amylolysis.

Ophthalmological Examination. Patient has a vision of 10/10 in each eye. Retinoscopy revealed a quarter diopter of myopic astigmatism; axis, horizontal. Phoro-

meter showed one degree of exophoria. Prisms give the strength of movements upward and downward about three degrees. The right eye has an outward strength of six degrees and an inward of the same amount. The left eye has an outward and inward strength equal to eight degrees. The fundus apparently is normal except that the veins are larger than usual.

Urinalysis on May 2nd revealed the following: Quantity passed in twenty-four hours, 1,620 cc; color, Vogel's scale, No. 3; transparency, perfect; odor and consistency, normal; reaction, 0.56° acidity; specific gravity, 1,029 at 15.5° C.; total solids, 109.46 grams; salts of HCl, greatly in excess; of H_2SO_4, in excess; of H_3PO_4, increased; of CO_2, normal; free NH_3, traces; carbamid, 3.4 per cent=55.08 grams; uric acid, 1.77 grams; ratio of uric acid to carbamid, 1:31.1; xanthin, hypoxanthin, present; creatinin, in excess; hippuric acid, present; urobilinurin-indican, slightly increased; albumin, absent; biliary acids, glucose, glycuronic acid compounds, absent. Microscopically distinguished, considerable amounts of crystals of uric acid, urates and calcium oxalate; mucous corpuscles; some polynuclear leucocytes; epithelium of prostate in moderate amount; of bladder and urethra in large quantities.

Blood Examination, May 2, 1901. (Microscopical.) (a) Fresh blood. Blood count, erythrocytes, 3,600,000 in 1 c.mm. blood; leucocytes, 7,000 in 1 c.mm. blood; proportion of leucocytes to erythrocytes in 1 c.mm. of blood, 1:514.

(b) Dried specimens of blood. Erythrocytes, small lymphocytes, mononuclear and polynuclear leucocytes, eosinophiles, neutrophiles.

Blood Examination, May 9, 1901. Alkalescence, 266.5 mg; NaHO in 100 cc blood; specific gravity, 1,057; hemoglobin, 78 per cent; blood count, erythrocytes, 5,100,000 in 1 c.mm. blood; leucocytes, 8,000 in 1 c.mm. blood; proportion of leucocytes to erythrocytes, 1:637.

Microscopically distinguished.—Normal erythrocytes, blood plates, small and large lymphocytes, polynuclear leucocytes, eosinophiles.

A great number of urinary and blood examinations were performed between May 9 and October 7, 1901. The urine on no occasion exhibited any abnormal constituents; its daily amount averaged 1,550 cc, its specific gravity, 1,029.5; its degree of acidity, 0.53; and its contents of carbamid never exceeded 3.5 per cent.

The only urinary elements permanently in great excess, those to which in greater part the high density seemed to be due, were the chlorids. In the twenty-four hours' urine of May 28-29, for instance, 12.09 grams of Cl were excreted. The patient's weight being at that time 65.5 kilograms, 0.1818 Cl were excreted for each kilogram of body weight. This is certainly in excess of the average, which amounts to 0.126 gr Cl per kilogram of body weight.

As the patient during that period was on a milk régime, to the exclusion of all other foodstuffs, the amount of chlorin which he ingested with the nutriment is calculated readily. The quantity of milk partaken of daily was 7,000 cc. In 1,000 cc of milk 1.7 grams of chlorin are contained, on the average. The patient ingested, therefore, 11.90 grams of chlorin every day, which corresponds about to its output by the urine in that time.

Determination of the Relative Urinary Toxicity. June 22, 1901. Narcoleptic condition between 11 a. m. and 4 p. m. (1) Night urine, 360 cc; acidity, 0.62°; density, 1,033. (2) Urine voided between 6 a. m. and 10:30 a. m., 310 cc (prior to attack); acidity, 0.48°; density, 1,028. (3) Urine voided between 4:30 p. m. and 7 p. m., 190 cc (after attack); acidity, 0.3°; density, 1,031.

June 23, 1901. (1) Night urine, neutralized by $HNaCO_3$, filtered, possessing a temperature of 30° C., was injected into a vein of the ear of a rabbit weighing 2,050 grams.

Prior to injection, rectal temperature, 38.4° C.

After injection of 30 cc, pupil unchanged; defecation.

After injection of 38 cc, myosis, respiration very rapid.

After injection of 50 cc, rectal temperature, 38° C., slight rigidity.

After injection of 65 cc, respiration, 50; pulse, 140; defecation.

After injection of 75 cc, emission of urine.

After injection of 83 cc, convulsions, opisthotonos, death.

Time, eight minutes. Consequently, $83 \times 100 \div 2{,}050 =$ 40.48 cc of night urine were necessary to kill one kilogram of animal.

(2) Urine voided prior to attack, treated as the night urine, of a temperature of 30.5° C. injected into an aural vein of a rabbit weighing 1,960 grams.

Prior to injection, rectal temperature, 39.2° C.

After injection of 18 cc, myosis perceptible.

After injection of 30 cc, rectal temperature, 39.3° C.

After injection of 35 cc, myosis complete.

After injection of 43 cc, defecation; pronounced tremor.

After injection of 50 cc, emission of urine.

After injection of 55 cc, respiration, 46; pulse, 152.

After injection of 65 cc, strong convulsions.

After injection of 68 cc, death.

Time six minutes. Consequently, $68 \times 1{,}000 \div 1{,}960 =$ 34.69 cc of antenarcoleptic urine were necessary to kill one kilogram of animal.

(3) Urine voided after the attack of somnolence, treated as the night urine, of a temperature of 30.4° C., was injected into an aural vein of a rabbit weighing 1,885 grams.

Prior to injection, rectal temperature, 40° C.

After injection of 40 cc, beginning of myosis.

After injection of 45 cc, rectal temperature, 40° C.

After injection of 50 cc, myosis more pronounced; respiration, 38.

After injection of 52 cc, rigor.

After injection of 57 cc, respiratory intermission.

After injection of 60 cc, death without convulsions.

Time, six minutes. Consequently, $60 \times 1{,}000 \div 1{,}885 =$ 31.83 cc of postnarcoleptic urine were necessary to kill one kilo of animal.

October 6, 1901. Narcoleptic condition between 10:50 a. m. and 5:30 p. m.

(1) Urine voided at 10:30 a. m., 125 cc; acidity, 0.54°; density, 1.025.5.

(2) Urine voided at 6 p. m., 150 cc; acidity, 0.45°; density, 1,033.

(1) Urine of 10:30 a. m., prior to attack, neutralized by $HNaCO_3$, filtered, possessing a temperature of 20.5° C., was injected into a vein of the ear of a rabbit weighing 1,620 grams.

Prior to injection, rectal temperature, 37.4° C.

After injection of 20 cc, respiration accelerated.

After injection of 30 cc, slight myosis.

After injection of 35 cc, tremor, great restlessness.

After injection of 38 cc, emission of urine.

After injection of 40 cc, respiration diminished, temperature, 37.5° C.

After injection of 50 cc, paralytic manifestations.

After injection of 55 cc, complete myosis, defecation.

After injection of 65 cc, respiration shallow, very frequent; pulse, 152.

After injection of 75 cc, convulsive phenomena.

After injection of 85 cc, convulsions, opisthotonos, death.

Time, twenty minutes. Consequently, $85 \times 1{,}000 \div 1{,}620 = 52.47$ cc of antenarcoleptic urine were necessary to kill one kilogram of animal.

(2) Urine at 6 p. m., first excretion after attack had abated, treated as the morning urine, of a temperature of 20.5° C., was injected into a vein of the ear of a rabbit weighing 1,675 grams.

Prior to injection, rectal temperature, 38° C.

After injection of 25 cc, slight myosis.

After injection of 30 cc, great restlessness.

After injection of 40 cc, complete myosis, defecation.

After injection of 45 cc, clonismus in extremities.

After injection of 70 cc, respiration 60, temperature 39° C.

After injection of 75 cc, heart pulsation 144.

After injection of 88 cc, convulsions, death.

Time, eleven minutes. Consequently, $88 \times 1{,}000 \div 1{,}675 = 52.53$ cc of postnarcoleptic urine were necessary to kill one kilogram of animal.

Conclusions.—Summing up the foregoing data, we find:

(a) Diurnally recurring morbid somnolence.

(b) Free perspiration on hands, feet and forehead at all times, and particularly so before attacks.

(c) Physical condition remains uninfluenced by the attack.

(d) Physiologic sleep does not refresh the patient.

(e) Weak, slightly hypertrophied heart.

(f) Dilated stomach and hyperchlorhydria.

(g) High urinary density and acidity.

(h) Urinary chlorids greatly in excess.

(i) Salts of sulphuric and uric acids, carbamid, creatinin, and calcium oxalat in excess in the twenty-four hours' urine.

(k) Diminished blood alkalescence; hemoglobin somewhat reduced in amount.

(l) Low degree of relative urinary toxicity before as well as after the attack of somnolence.

Inasmuch as the attacks of morbid somnolence never occurred until the twenty-ninth year of the patient's life, and as he at no time met with an injury of moment, we have to conclude that a toxicosis of some kind stands at their foundation. Ectogenesis of a specific toxic material may at once be excluded, as the patient is a total abstainer from alcohol and tobacco, as the seizures occur independently of the administration of drugs, and

as the attacks continue unmodified during the last five months in which period he ingested nothing but milk.

There is apparently nothing left but to assume the autochthonous production of a toxic substance causing narcolepsia. To what degree, however, is this assumption justified?

The patient is not now, nor has he since his childhood been afflicted with an infectious disease; his liver performs its functions in a normal way, cholemia is not present; renal insufficiency and renal disease of any character, as shown by the numerous urinary examinations, must be excluded; the supply of oxygen to the blood is normal, and there is no evidence of retention of carbon dioxid. No sign points to an enterogenic toxicosis. Indoxyl-potassium-sulphate, though slightly increased on some occasions, never occurred in abnormal quantities, and acetone and ethly-diacetic acid were at no time detected in the urine. None of the data obtained are symptomatic of a histogenic toxicosis. Uric acid, or any of the purin bodies, were not found in such quantities as to support the assumption of an abnormal nucleolysis; and abnormalities of specific "internal secretions" could not be demonstrated.

A number of authors have tried to fasten the cause of various mental diseases upon an autotoxicosis. We are already aware of the fact that some acute psychoses form an integral part of the clinical picture of autointoxication.[4] They generally disperse in the ratio in

[4] *Acute confusional insanity* and similar disorders mentioned by writers on the subject of autointoxication, rather seem to be the consequence of toxicoses than of intestinal autointoxications.

which the other autotoxic phenomena disappear. Convincing facts as to the autotoxic origin of certain chronic psychoses—in spite of a superabundance of theoretically pertaining material—has hitherto not been furnished.

PERIODICAL VOMITING.

Periodical vomiting, first described as a disease *sui generis* by von Leyden (19), has repeatedly been considered as arising from an intestinal autointoxication. Doubts may be entertained as to the correctness of von Leyden's contention. Again, positive evidence to establish the dependence of the affection upon an entero-autotoxicosis has not been brought forward. Clinically, the individual attacks greatly resemble those of typical cases of intestinal autointoxication. LeRoy (20) attributes it to an autointoxication from the small intestines. Edsall, who reported some observations on recurrent vomiting in children, (21) is of the opinion that cryptogenic acid intoxication is one of the factors in the causation of this disorder.[5]

A case diagnosed by some experienced clinicians as one of periodical vomiting came under my observation in August, 1896. The patient, a woman, 44 years old, was affected with attacks of vomiting lasting from ten to thirty hours, and recurring every second or third day. The attacks continued for a period of almost two months and were accompanied by marked chills, severe headache and pressure in the back. Occasionally, paroxysms of

[5]Valagussa (Il Policlinico) maintains that recurrent vomiting occurs independently of gastrointestinal diseases, that it is a metabolic disorder affecting children with inherited uric acid diathesis, and that it may be looked upon as the equivalent of gouty paroxysms.

pain in the epigastrium, radiating to the dorsal region, preceded the vomiting. The blood showed no evidence of malarial disease; the urine, which was examined daily, invariably contained a small amount of glucose, never more than from 8 to 12 Gms in the twenty-four hours; in spite of her one-sided diet, consisting of milk and milk preparations, and her progressive emaciation, acetone bodies were not found on any occasion. The feces exhibited large amounts of free fat. Pancreatic disease—with pancreatic calculi, presumably—was diagnosed to underlie the vomiting seizures. The concretions could never be demonstrated in the stools as, probably, they were of small size and disintegrated in the enteric canal. The subsequent history of the case, the almost synchronous cessation of the glycosuria, of the augmented fat excretion and of the vomiting, tended to confirm my original diagnosis.

This case of periodical vomiting proved neither an affection *sui generis,* nor one of autotoxic origin, certain phenomena pointing toward it notwithstanding. After all, many, if not all instances of cyclical vomiting considered morbid entities, and due to intestinal autotoxicosis, may be nothing but the chief symptom of a tangible disturbance.

ASTHMA DYSPEPTICUM.

Asthma dyspepticum, a symptom-complex generally ascribed to nervous reflexes through the pneumogastric, has, by some, been attributed to autointoxication. The disturbance is not only of rare occurrence, but when present often remains unrecognized. The symptom-complex is not very definite; it presents obvious similarity with that of cardiac asthma, and also, to a certain

degree, with angina pectoris. According to Albu (22) the clinical course of asthma dyspepticum points to its toxic foundation. It appears immediately after an alimentary disturbance and passes away with the removal of its causes.

Certain instances of aerophagia may easily be taken for asthma dyspepticum. During the presence of air in the stomach or in the lower portion of the esophagus, the patient may exhibit, aside from the gastric symptoms, as pointed out by me (23), pronounced anxiety, shortness of respiration, a feeling of impending suffocation, cardiac palpitation, cephalalgia and vertigo. Taking also into consideration that all these phenomena subside almost immediately after removal of the cause, we find that the symptom-complex of aerophagia, as a whole, may closely resemble that of asthma dyspepticum.

It seems that the term "asthma dyspepticum" is not the proper one for this symptom-complex of manifold causation and that its suposed autotoxic origin still awaits verification.

TETANY.

A number of modern clinicians look upon tetany as an expression of autotoxicosis. Albu (loc. cit.) maintains that this affection is the best illustration of a gastrointestinal autointoxication. Tetany obtains mostly in the presence of gastrectasia, enteritis and helminthiasis —in conditions characterized by or concurring with abnormal fermentative and dissimilative processes. It is of infrequent occurrence in affections like gastric blennosis, gastric ulcer, etc. According to Monti (24), quickly appearing and subsiding autointoxications call forth tetany, while chronic and prolonged autointoxica-

tions (the probability of which, if not a succession of a series of acute attacks, is dubious) give rise to pathological myotony.

The paroxysm manifests itself by bilateral, symmetrical, tonic or clonic spasms of the voluntary muscles, beginning at the distant ends of the extremities and extending to the proximal parts of arms and legs. The muscles involved are hard, and are very sensitive to pressure. Edema of the limbs is not uncommon. Elevation of temperature occurs in about half the cases. The attack usually lasts for some minutes, but it may continue for hours or days, and even during sleep. Occasionally, the paroxysms supervene with a certain degree of regularity. Pain in the head, neck and dorsal region are usual concomitants. Sometimes, unconsciousness prevails during the attack.

The paroxysm-like occurrence of the phenomena, and the fact that the injection of certain substances, such as chloroform, ergotin or mucin, is followed by artificial tetany, lends color to the assumption of the autotoxic causation of tetany. However, in spite of some work done in this direction, no chemical substance to which could be ascribed tetanygenous activity has as yet been isolated.

After all, Kussmaul's (25) contention that tetany is the result of dehydration of the organism may be true. This would result in disturbance of the intraorganic osmotic equilibrium and an impaired electrical conductivity of the blood serum,[6] facts about which Kussmaul

[6]Kaufmann (Remarks on Gastrosuccorrhea and Tetanic Attacks Occurring with Chronic Ulcer of the Stomach. Am. Jour. Med. Sci. April, 1904), by maintaining that in the majority of cases of gastric tetany increased quantities of chlorin, which enter into the composition of gastric juice, are withdrawn from the blood, again confirms this contention.

could not have known anything when he first propounded his theory in 1872. We will see elsewhere that disturbances of the normal intrabiontic molecular concentrations may give occasion to all the manifestations which are still considered chemico-autotoxic in character.

INFANTILE CONVULSIONS.

There undoubtedly exists a relationship between convulsions and alimentary disturbances in children. However, we possess little proof, if any, that this connection bears an etiological character. It is quite possible that an ectogenous poison, introduced into the gastrointestinal canal, is the cause of both these manifestations.

Nevertheless, the theory of the autotoxic origin of infantile convulsions, or, as it is also called, of infantile eclampsia, gains new advocates every day. There is hardly any modern pediatrist who has not assigned the cause of some of his cases of infantile convulsions to autointoxication. They may occur in a syndrome characteristic of acute autointoxication, and may at times exhibit great resemblance to tetany. Again, helminthiasis, which also indicates an abnormal condition of the alimentary tract, has frequently been charged with the causation of infantile eclampsia.

CHLOROSIS.

Chlorosis, in the opinion of observers like Duclos (26), Bouchard (loc. cit.), Conturier (27) and Charrin (28) in France; Clark (29) in England; Nothnagel (30) and, in a certain sense (cessation or deficient "internal secretion"), also v. Noorden (31), in Germany; and Forchheimer (32) in the United States, may be the consequence of autotoxic process.

Experimental proof of this assumption has hitherto

not been brought forward. The conception of the autotoxic basis of chlorosis is, nevertheless, justified for more than one reason. However, the term intestinal autointoxication, denoting a more or less paroxysmal disorder, does not adequately express the condition underlying chlorosis, which must be of an exceedingly chronic nature.

PERNICIOUS ANEMIA AND LEUCEMIA.

Among a vast number of etiological theories, that of intestinal autointoxication was also brought in in connection with the grave blood diseases, pernicious anemia and leucemia. These pathological states may be considered specific manifestations of an autointoxication in a very general sense. They do not seem to be the outcome of an intestinal autointoxication, as the clinical pictures which they exhibit show very little semblance to that of a true enterogenous toxicoses. Vehsemeyer (33), who studied the clinical histories of 600 cases of leucemia, holds the opinion that the condition arises from tox-albuminoids contained in the alimentary tract. Koettnitz (34) furnishes some proof according to which leucemia occurs on the basis of chronic peptonemia, however, a rational explanation concerning the autotoxic production of leucemia was, as yet, not attempted.*

CYSTINURIA AND DIAMINURIA.

Cystinuria generally is associated with diaminuria. Cystin is a decomposition product of proteid material. According to Möerner (35) it may result from hydrolysis of keratin. Penta- and tetra-methylendiamin, found by Baumann and v. Udransky (36) in urine containing

*On the other hand proof is not wanting that leucemia is the result of some infection or autoinfection.

cystin, are identical with Brieger's cadaverin and putrescin, which are derived from putrefying meat. The fact that diamin bodies have also been demonstrated in the intestinal excretions of cystinurics, points to specific intestinal decomposition processes in individuals thus affected.

Cystinuria appears to be an expression of retarded metabolism due to imperfect intrasystemic oxidation. The diamin bodies in cystinuria are of enterogenous formation. It is not known whether they exert a poisonous action upon the system in the amounts in which they usually occur. However this may be, various concomitant phenomena, as neuralgia and rheumatic affections, anemia, etc., appear regularly in cystinuria.

INTESTINAL ACETONURIA AND DIACETURIA.

The question of acetonuria and the frequently associated diaceturia is not definitely settled, von Noorden's contention notwithstanding (37). In acid intoxication, which will be dwelt upon hereafter, acetone and diacetic acid seem to be often the result of the disintegration of body material, and while they themselves are not causative of any pronounced toxic phenomena, their presence points to a toxic state of the organism. Intestinal acetonuria and diaceturia appear as the consequence of abnormal digestive processes and are especially prominent features after continued abstinence from carbohydrate ingesta, and after prolonged ingestion of considerable amounts of fatty material. That diminished carbohydrate feeding is not the sole cause of acetonuria, as maintained by von Noorden, is shown by the following case:

The patient, 45 years old, has been a diabetic since

his 39th year. Between March and May, 1903, his affection, which had been of a comparatively mild type for five years, began to assume a grave character. On February 22, 1903, while under the diet which he pursued for the past three years and which contained 150 Gms of carbohydrates per day, he weighed 147½ pounds, and his urine contained neither glucose, acetone nor diacetic acid. On May 10th his weight had declined to 146¾ pounds, and his urine (the amount of which had not been ascertained) exhibited 1.5 per cent glucose, but the tests for acetone and diacetic acid showed neither. On May 25th, while under a rigid meat-fat regime, he excreted 4 per cent, or 90 Gms, of glucose, but no acetone or diacetic acid. On June 8th the diurnal amount of excreted glucose had diminished somewhat, but there were traces of acetone, and the ferric chlorid reaction was fairly pronounced. His weight was 145¼ pounds. About June 25th he consulted Prof. von Noorden at Frankfort, who informed me that he had found 2.3 per cent, or 56 Gms, glucose, and 1.5 Gm acetone in the 24 hours' urine, and that the ferric chlorid reaction, although faint, had occurred. Upon his return on September 13th he weighed 144 pounds, his urine contained large amounts of glucose and some acetone, but no dicetic acid. On September 23d he excreted 181.6 Gms glucose, a small amount of acetone, but no diacetic acid. On September 25th, after two days of a green vegetable and fat (butter) diet, as advised by von Noorden, he excreted but 83.4 Gms glucose, but over 2 Gms acetone and also some diacetic acid. On September 29th his weight had declined to 143½ pounds, the glucose output to 54.97 Gms, the amount of acetone

had not materially changed, the ferric chlorid reaction was positive. Keeping the patient under a very rigid diet (complete exclusion of carbohydrates, diminished amount of albumin, no egg albumin, only the yolks), he weighed 145¼ pounds on October 5th, and had excreted during the previous 24 hours about 43 Gms glucose, and traces of acetone; diacetic acid was not detected. Withdrawing all fatty substances except the yolks of eggs, he weighed on October 12th 148¾ pounds. The glucose output had diminished to 38.18 Gms; acetone had entirely disappeared. Diacetic acid was not present.

Olive oil added to the diet at a later date was followed by a slight output of acetone; addition of butter, tried on various occasions, caused pronounced acetonuria. Beef fat, in the amounts ordinarily employed, remained without influence upon the acetone excretion. The patient weighed 152½ pounds on November 30th, and passed as little as 10 Gms glucose on January 10, 1904. His urine remained entirely free from acetone until the end of February. Since this time, small amounts of acetone as well as of diacetic acid are met with occasionally. His present weight is 149½ pounds. Since the middle of October, 1903, his diet consists of meat and fish and their natural fat substances, of gelatin, green vegetables, almond cake, coffee and some brandy. The daily caloric deficit is made up by the yolks of eggs, of which he had as many as fourteen per day. These are incorporated into gravies and vegetables, and added to the coffee and brandy.

I may add that this case does not stand isolated in my experience.

Acetone and diacetic acid, occurring in quantities ap-

preciable by clinical tests, are always of more or less pathological significance. However, their presence in the urine of diabetics who have been under a rigid proteid-fat diet for a prolonged period must not be invariably interpreted as prodromic of diabetic coma. I have seen many cases in which acetone and diacetic acid continued to be egested in excessive amounts for months without any toxic manifestations.

On the other hand, a number of diseases and complications, most of which have been mentioned before, are by some considered autotoxicoses due directly or remotely to acetonemia and diacetemia. Apart from the probably frequent nonenterogenous formation of acetone and diacetic acid, it is yet dubious whether any toxic action can be ascribed to these substances in the amounts in which they have usually been met with in the blood. A series of experiments in man and animals, conducted by me, evidenced the relative innocuousness of acetone and diacetic acid, and the probability of their nonparticipation in the production of the pathological phenomena attributed to them.

We can, however, not err very much by assuming that the occurrence in excess of acetone and diacetic acid in the urine is the consequence of certain anomalous processes, which latter also stand at the foundation of the various toxic manifestations.

Besides the above mentioned disturbances, the causation of some other diseases and complications has been assigned to enterogenous poisons. A few of these diseases were ignored, as their nonintrabiontic origin is too obvious; others, presumably of autotoxic production, but not ascribed to intestinal autointoxication, will be considered later.

Chapter V.

CATABOLIC AUTINTOXICATION.

1. *Definition and Scope.*

Under catabolic autointoxication I comprise all processes which are the supposed direct or mediate result of retained and accumulated, of incompletely or perversely converted, or unattenuated, or non-dissociated, or irregularly combined substances derived from beyond the stage of anabolism. Contrary to the intestinal poisons, there should prevail no uncertainty as to the intrabiontic origin of these supposedly toxigenous products. The catabolic autotoxicoses, hence, may be considered the autointoxications par excellence.

The catabolic autointoxications are manifold in nature and degree. In the abnormal retention of carbonic anhydride in the blood is exemplified the most simple and, at the same time, the most authentic of all catabolic autotoxicoses. Very close to this, and also highly authentic, though somewhat more complicated, are the autointoxications following the partial or complete suspension of the respiratory and other functions of the skin. While the respiratory gas interchanges by the medium of the skin, compared with those taking place in the lungs, are diminutive, it must not be disregarded that a portion of such solid metabolic products as carbamid, tartronylcyanamid, fatty acids, leucin, tyrosin, etc., leaves the organism by way of the integument.

Suppression of the normal activity of the skin and subsequent autotoxic phenomena are noticed after ex-

tended burns or scalds of the skin, after varnishing it with resinous substances, in ichthyosis, psoriasis universalis and in any affection involving an extensive portion of the integument.

According to conclusions reached by von Dieterichs (38), elevation of temperature occasions disintegration of the cellular elements of the blood and tissues. This is followed by the production and accumulation of various toxins. One may be tempted to hold the hypothetic blood changes accountable for the autotoxic phenomena likely to ensue after burns of the skin; recalling, however, that a similar toxic state may arise after covering of the cutaneous surface with an impermeable varnish, in which, consequently, there does not enter the element of excessive high temperature, we are forced to conclude that the pathological manifestations in the wake of suppressed cutaneous respiration and secretion are primarily due to the retention of excrementitious material continuously exhaled and discharged by the normal skin.

Besides these forms of retention autotoxicoses, the histolytic autotoxicoses, including autolysis, acidosis and nucleolysis; the histoenzymic autotoxicoses, and the combined retention-histolytic autotoxicoses are comprised in the catabolic autointoxications.

2. *Histolytic Autotoxicoses.*

(*a*) *Autolysis.*—The living cell secerns the elements which by gradual hydrolysis may destroy its own protoplasmatic material. This autofermentative process is probably the normal manner in which destruction of the body-protoplasm ensues.[1] Its direct bearing upon the

[1] If the hypothesis of the "antibodies" be well founded, the

question of autointoxication seems mostly an academic one; however, it may become of special importance in its relation to the histolytic autotoxicoses in general. The plasmolytic, adipolytic and nucleolytic processes which may give rise to acid intoxication and excessive formation of purin bodies, respectively, very likely are themselves the sequence of autolysis. Again, anomalous histoenzymic activity may be ascribed to autofermentative changes in the various gluandular cells, or to any interference with the "internal secretions" by the autolytic ferment.

Inasmuch as autolysis seems to have but an indirect connection with autotoxic phenomena, and as some of its eventual direct results, forming substrata of various autotoxicoses, are dwelt upon seriatim in the following, I shall forego further discussion of autolysis per se.

(*b*) *Acidosis.*—Under acidosis or acid intoxication is understood a condition caused by long-continued overproduction of acid intermediary substances and concurring loss of alkaline principles. The excessive amount of acid compounds may be distributed in all body-fluids or may accumulate in a certain organ (or in a certain type of organs). In the latter eventuality the toxic effects of acidosis are more of a local nature, and seem of little general importance. However, if large amounts of acids are passing into the body-liquids, serious results may be occasioned. Free acids, originating during the

---

presence of specific "antiferments" would afford protection against the autolytic processes of and in the tissues; their absence, on the other hand, being followed by disintegration of tissues and organs, could be held responsible for almost every wasting disease.

metabolic processes, are soon neutralized by combining with certain alkaline bases which always occur in sufficient quantities in the healthy state of the organism. The most important of these bases are the sodium carbonate of the blood and ammonia. The danger arising from acid intoxication cannot be ascribed to a specific chemical toxicity of the intrabiontically formed acids, but must be assigned to the continuous withdrawal of alkalies from the tissues and their non-renewal.[2]

We will appreciate the peril to which the organism is exposed by the excessive demand of the acids upon the alkali supply, when we know that, apart from the bony structures, there are only about one per cent of mineral matters contained in the body, and that a certain amount of alkali is absolutely essential for the performance of tissue respiration and for the maintenance of the metabolic as well as the physico-electrical equilibrium.[3]

[2]The dihydrogen sulphate yielded by disintegrated albuminous substances will accumulate in the organism when there is a lack of alkali and to this acid Bunge (Lehrbuch der Physiolog. Chemie, 1898, S. 97) ascribes the destruction of body material and the rapid death of certain experiment animals.

[3]Magnus-Levy (Die Oxy-Buttersaeure und ihre Beziehungen zum Coma diabeticum, 1899) admits that the alkali contents of the body may be somewhat diminished by elimination of the acids in the form of neutral salts and that even the slight withdrawal of alkali may give rise to untoward results. He contends, however, that the body-alkali is insufficient to neutralize the continuously produced acid, that the organism cannot spare much alkali for any length of time and that almost the entire oxybutyric acid combines with NH_3. This contention is certainly true as far as it concerns the fasting animal or the organism in which little or alkali-poor nourishment is introduced. In individuals subsisting on regulation diet, alkali sufficient to neutralize the acids is introduced with it as a rule.

The acids which have been oftener considered in connection with acidosis than any other are beta-oxybutyric acid, diacetic acid and acetone. These three interrelated substances, designated as "acetone bodies" by Geelmuyden (39), very likely are derived from one another or from a common source. The supposition that the carbohydrates give rise to the production of acetone has long since been abandoned. Rosenfeld (40), Hirschfeld (41) and von Noorden (37) have observed that in non-diabetics acetonuria will particularly ensue when the carbohydrates are either not at all or but sparingly ingested.

The subsequent conception concerning the origin of acetone bodies from albumin—either from disintegrating body-albumin or from ingested proteids—has also proved scientifically untenable.

Oxybutyric acid, hence, is either formed from fatty substances or it originates by synthesis. Geelmuyden (l.c.) has already pointed to both possibilities. However, he has not designated the fat as the mother substance of acetone. Magnus-Levy (l.c), who, with the assistance of the evidence at our disposal, cannot decide whether the oxybutyric acid is due to fat decomposition or to a synthetic production, treats at some length on the eventuality of the latter.

For our present purpose it suffices to know that the acetone bodies are of true intrabiontic formation and that the occurrence of acidosis has been demonstrated in conditions of absolute inanition and prolonged underalimentation, in grave infectious diseases, in various gastric disorders, in diabetis mellitus, scorbut, carcinomatous cachexia, progressive anemia, leucemia, etc., in short,

in such states in which considerable loss of body-substance is noticed.

Besides acidoses of known origin, there is a certain acute, apparently cryptogenic, form of this condition. This acid intoxication, *sui generis,* as it is called, according to Kraus and Honigmann (42), in all likelihood is an accidental intestinal autotoxicosis. As there exists an etiological connection between certain digestive disturbances and acid intoxication, it is possible that some instances of non-diabetic acidosis are of intestinal origin. (Intestinal diaceturia.)

Acid intoxication is recognized by the appearance of oxy- and amido-acids and by large amounts of ammonia in the urine. When oxybutyric acid is excreted in larger amounts, the NH_3 output is also augmented, but the increase of both substances does not occur in the same ratio. The NH_3 elaborated from disintegrating albumin is but a substitute for the fixed alkalies in the organism and it is utilized to the extent only of covering an eventual deficiency of the latter. As the available amount of fixed alkalies is dependent upon their introduction into the organism, their supply in large amounts should cause diminution of NH_3 excretion even in the presence of pronounced acidosis.[4]

A provisional diagnosis of acidosis may be entertained when the urine after ingestion of five grams sodium

[4]Upon this contention Stadelmann (Arch. f. experimentelle Pathologie und Pharmacologie, XVII and Deutsch. Arch. f. Klin. Medicin, XXXVII and XXXVIII) has based the modern alkali therapy for acidcoma which in my hands proved a decided failure when the latter was fully developed (Coma diabeticum, its treatment. Jour. Am. Med. Ass., Dec. 8, 1900).

bicarbonate every hour, repeated for three hours, still exhibits an acid reaction.

Direct indicators of the degree of acid intoxication are the quantitative determination of the blood-ash, or the determination of the proportion of acids and fixed bases in the excretions.

There is no fixed and unvarying syndrome in all the cases of acidosis. The reasons for this are manifold: the anomalous products of metabolism may not appear in the same amount of rapidity; they may be transformed into innocuous substances in varying periods; the quantity of available alkali in the body may be different; the direct effects of acidosis may act in combination with those of its causes (Senator); there may be an intercurrent disease; or another type of autointoxication may supervene.

Certain terminal manifestations of the nervous system, including somnolence and coma, are still the most fixed (in themselves) and unvarying phenomena in the train of acidosis, but whether the latter is their direct and sole causative factor or whether other circumstances contribute towards their production, has been determined in but few specific instances.

The limits set to my discourse prevent me from going into further detail concerning the present views on acidosis. I wish to state, however, that beta-oxybutyric acid is not that all-important factor in the production of acid intoxication which it is generally held to be. *All acid principles seem to participate in the causation of acidosis.* These acids may be the result of the normal or anomalous conversion of *any* type of nutriment, or they may be due to the disintegration of protoplasmic as well

as fatty body-substances, or to a combination of any and all these factors. They interest us on this occasion in as far as they are the outcome of catabolic occurrences; intestinal acetonuria and diaceturia have already found due consideration.

At the foundation of acidosis seems to stand a faulty alkali supply. In the normal state, the withdrawal of alkali (for neutralizing purposes) is quickly followed by a renewed supply. Such renewal, we understand, does not take place, or to an insufficient degree only, in fasting organisms or in underfed individuals. On the other hand, how are we to explain the alkali deficit in the face of abundant and even overabundant alkali ingestion?

An explanation of this phenomena may be deduced from some of my own investigations (43); I found that:

(a) The blood, under normal conditions, possesses a certain inherent alkalinity. The degree of alkalescence possibly varies slightly for certain periods of the twenty-four hours, but the influence of the ingesta upon these variations is neither a material one nor always determinable.

(b) The degree of blood alkalinity is normally not affected by the *quantity* of the ingesta. The *quality* of the nutritives may normally contribute toward the rise and fall of the blood alkalinity, but only to a very limited extent.

(c) A number of drugs (alkalies) effect the alkalinization of the urine without causing a corresponding increase in the degree of blood alkalinity.

(d) The transitory augmentation of blood alkalinity, recurring mostly during certain hours of the afternoon, seems to be the result of certain innate processes which

apparently proceed independently of the ingestion of foods or drugs.

These observations have demonstrated that certain amounts of alkali either do not enter the general circulation at all, or remain therein for a very brief period only. Normal blood possesses a certain degree of alkalescence which is automatically maintained. In acidosis, even, I repeatedly found the blood alkalescence but slightly impaired. Maintaining that faulty alkali supply is primarily responsible for the acid intoxication, we must infer that the alkali either does not reach the blood current at all, which would explain the continued acid reaction of the urine heretofore mentioned as a provisional diagnostic point, or else, the alkali passes in and through the blood without entering the cellular structures in which the acid formation has ensued.[5] Both eventualities are explainable on physical and physicochemical grounds.

(*c*) *Autotoxicosis by Nucleolysis.*

The substances derived by nucleolysis, the alloxuric or purin bodies and xanthin bases, when produced in excessively large quantities and retained in the organism, may be associated with a more or less pronounced symptom-complex. Abnormal nucleolysis, retention of the dissimilation products, and the resulting pathological

[5] In acidosis the neutralization afforded by the ingestion of large amounts of sodium bicarbonate is apparently confined to the acid contained in the intestinal canal. In case, even, that the alkalescence of the blood becomes enhanced after alkali therapy, which, at the best, can be of a very transitory character only, the neutralizing effect, if above contention be true, is not transmitted to the real seat of the acid production and intoxication; the muscle cells and the adipose tissue.

manifestations, have been considered a true autointoxication by a number of clinicians.

Uric acid, after all, appears to be the most important product of nucleolysis, in the normal as well as in the pathological state. There are three sources of uric acid in the mammalian organism. First, the leucocytes, which are the main source under certain conditions; second, the nucleins of the food, more particularly the nuclein bases; third—probably only under pathological conditions—the catabolism of body-cell nuclei. The xanthin bases are yielded by the same sources.

The toxicity of uric acid is still an unproven factor;* that of the xanthin bases, on the other hand, is pretty well established. Caffeine, the active principle of coffee, is a xanthin base. Chemically it is known as trimethylxanthin, $C_8H_{10}N_4O_2+H_2O$.

The symptoms of chronic coffee poisoning, such as neurasthenia, cephalalgia, cardiac palpitation, etc., are due to this alkaloid. It stands to reason that if an ectogenous xanthin base occasions true toxic phenomena, one of metabolic production, under suitable conditions, may give rise to a similar syndrome.

Contrary to former belief, uric acid usually occurs in normal amount and proportion in the urine of the gouty individual. The value of the urine in the recognition

*That Ebstein and also Pfeiffer found uric acid accumulated in the tissues, to act as an aseptic necrobiotic poison, and that Stadthagen (Virch. Arch. 109) observed grave toxic manifestations in a patient affected with leucemia after administering six grams sodium urate, is certainly not evidence enough to consider uric acid the materia peccans in the sense of Haig or some other uric acid champion.

of the lithemic state is, therefore, often chimeric. However, uric acid, the presence of which in the blood of healthy persons was never positively demonstrated, occurs in appreciable quantities in the blood after ingestion of thymus, in leucemia, in gout and in many instances of nephritis.[1] While blood uric acid is absolutely and relatively augmented after feeding of thymus and in leucemia, its production is not increased in gout or nephritis. The occurrence of uric acid in the blood of the two latter affections is undoubtedly due to its retention therein. In nephritis, the accumulation of uric acid in the blood may be ascribed to the insufficiency of the diseased kidneys; in gout, on the other hand, uric acid retention in the blood is the consequence of specific conditions heretofore not taken into consideration. These conditions, according to Camerer (44) and Weisz (45), are dependent upon the presence and quality of the physiological uric acid solvents.

In 100 Cc of gouty blood there are contained about six milligrams of uric acid. If uniformly distributed, the blood of a gouty individual weighing seventy kilograms holds but 4.2 grams of this catabolic product.

Weisz opines that in certain cases of leucemia and nephritis more uric acid is circulating in the blood than is in the blood of the gouty, and that it is not thrown

[1] We should distinguish between uricacidemia, always a secondary occurrence, and uric acid diathesis—a more or less hypothetical condition defined by Ebstein as that pathological disposition of the human organism, by which without other demonstrable functional or organic primary disturbances, and particularly in the absence of any respiratory insufficiency, more uric acid is produced than can ever be found in the normal state.

down as in the gouty condition. The precipitation in these instances seems to be averted by the presence of certain substances contained in the blood. Similar substances apparently exist in the blood of the normal individual. The solubility of uric acid in the organism appears greater than in water. The uric acid-dissolving properties of normal urine are from ten to forty times greater than those of an equal volume of water.

Uric acid is soluble in comparatively large proportion in serum derived from a gouty person. Hence, the assumption seems justified that in gout the saturation with uric acid is a local process only, depending upon local deficiency in dissolving properties. A consequence of this is the local deposition of the uric acid salt.

Besides the causation of gout, uric acid has been accused of being the sole or contributing factor in the production of a variety of pathological states. Neurasthenia, hysteria, chorea and epilepsy; hay fever, asthma and bronchitis; gastricisms; Raynaud's disease, anemia, paroxysmal hemoglobinuria; rheumatism; nephritis; diabetes, etc., at one time or another, had been looked upon as due to the influence of uric acid. Augmented uric acid excretion, and for that matter abnormally large amounts of other nucleolytic products, have occasionally been met with in these diseases; in some instances there exists, apparently, a certain relation between the latter and the increased output of the former, which does not imply, however, that any of the nucleolytic substances must of necessity stand at the foundation of those pathological states.

My standpoint in this question, briefly stated, is the following:

(a) Increased catabolic nucleolysis itself is already the result of an autotoxicosis (probably autolysis).

(b) The amount of uric acid may serve as a general indicator of the intensity of the nucleolytic processes, but it is not always the predominating product of nucleolysis.

(c) Some diseases and disturbances may occur secondary to augmented catabolic nucleolysis, but they are very rarely secondary to the nucleolytic products per se.

3. *Histoenzymic Autotoxicosis.*

Under the designation histoenzymic autotoxicosis I comprise not only the phenomena due to pathological histoenzymes in the sense of Schmiedeberg, but all those abnormal conditions which may be assigned to anomalous "internal secretions."

Much attention has been devoted to this subject of late. Sajous in a voluminous publication (46) has given some novel interpretations to various pertaining experiments and phenomena. It is, however, beyond the scope of this communication to enter into a discussion of the various deductions and conclusions advanced therein.

The normal excretory functions of the ductless glands: pancreas, thyroid, parathyroid, thymus, liver, spleen, salivary glands, ovaries, adrenals, pituitary body, seem of utmost importance for the proper conduct of the vital processes. Perverted activity of any of those organs or suppression of any of their internal secretions, may effect specific morbid states.

Among the presumably histoenzymic autotoxicoses may be classified: Graves' disease, the consequence of abnormally increased, myxodema, the result of suppressed thyroid activity; pathological adipositas after

removal of or morbid changes in the sexual glands; Addison's disease, an affection of the supra-renal capsules; acromegalia, a diseased condition of the pituitary body, and others.

It is not altogether improbable that a considerable number of pathological conditions—mainly those of a chronic nature—ensue on the basis of a histoenzymic anomaly; yet, in spite of the enormous amount of labor that has been spent on the subject of "internal secretion," many of the pertaining hypotheses and assumptions still await clinical and experimental confirmation.

4. *Combined Retention-histolytic Autotoxicosis.*

In a certain sense, most catabolic toxicoses are to some degree retention autointoxications. In uncomplicated instances of autointoxication, the toxic phenomena are as a rule displayed only while the metabolic products are retained in the system, the phenomena abate as the retention products and specific products are transformed or excreted. However, the products and specific blood conditions, due to perverted autolysis, plasmolysis, adipolysis, nucleolysis, and anomalous glandular activity are supposed to exhibit a certain chemico-toxicity, that is to say, their toxic nature is considered the primary and most potent factor in the causation of autointoxication.

On the other hand, in the combined retention-histolytic autointoxications, among which are counted cholemia and uremia, the prototypes of autointoxication, the pathologic manifestations are due in the first instance to the retention *per se* of *normal* metabolic products.

Cholemia appears as the result of obstructed outflow of bile from the liver or the bile-ducts to the common bile-duct and the intestine. It is met with as an accompanying condition in a variety of disorders. The reten-

tion of the biliary constituents in the blood renders this more or less poisonous. Taurocholic and glycocholic acids *per se,* or in combination with sodium as they commonly occur, possess excessive toxic qualities. In a hundred parts of bile there are contained 0.87 parts of taurocholate of sodium, and 3.03 parts of glycocholate of sodium. Even comparatively small amounts of bile are therefore poisonous.

The symptoms of cholemia, frequently called "biliousness," when in the milder form, i. e., the icteric condition, occurrence of large amounts of bile pigments in the urine, clay-colored feces, malaise, coldness and aching of limbs, yellow-furred tongue, chilliness, headache and vertigo, tinnitus aurium, blurred vision, slow respiration, anorexia, nausea and vomiting, occasional diarrhea, the now and then occurring decline of body-temperature, and in grave cases stupor, coma and convulsions, are nothing else than the manifestations of an autointoxication. These toxic phenomena are due—as far as we know—to the *retention of normal intrabiontic products.*

While the autotoxic state is in progress and at its height, taurocholate and glycocholate of sodium appear in diminished amounts in the urine; as soon, however, as the quantity of urinary bile salts reaches again its normal ratio, or is increased beyond this—as is usually the case after retention had occurred—the constitutional symptoms will disappear rapidly.

The other combined retention-autotoxicosis, uremia, the most important and most typical of all autointoxications, will be discussed later.

Chapter VI.

CRITICAL CONSIDERATIONS OF THE AUTINTOXICATIONS.

1. *The Indefinite Use of the Terms "Autointoxication" and "Autotoxicosis."*—The literature on autointoxication abounds in incorrect usages of these terms and all they imply. The toxic effects of tainted food, the infectious and autoinfectious processes and numerous mostly deuteropathic conditions are still designated frequently as autotoxicoses. I have pointed out elsewhere, however, that we cannot assume the existence of an autotoxic process, unless we have good reason to presume that the cellular energy of the organism has participated in the production of the toxic factor. As a matter of fact, most abnormal conditions, etiologically assigned to intestinal autintoxication, are due to intoxication of an ectogenous nature. The various diseases and complications enumerated in the chapter on "Intestinal Autointoxication" are genuine autotoxicoses only if the cells of the gastrointestinal mucosa have been actively engaged in the production or non-attenuation of their causative factors. Under this active participation of the cells of the alimentary canal I do not understand the part which they play in normal digestion, but all the energy which they evolve beyond that, be it directly or remotely, by normal (prolonged) operation or by anomalous processes. Viewed in accordance with this conception, but few of the "intestinal autotoxicoses" can be declared as

genuine autochthonus—in the light of our present knowledge.

2. *The Biological and Chemical Methods for the Demonstration of Autintoxication.*—Positive evidence as to the real causative factors of the various symptom-complexes considered autotoxic in origin is still wanting in almost every instance. By the *clinical* acceptation of the autotoxic origin of a given disease it is by no means proven that it has really arisen on the basis of an auto-intoxication. The clinical evidence of an autointoxication rests upon the similarity of its course and symptoms with those of known intoxications, and upon the exclusion of an ectogenous causative factor. While, no doubt, in many instances an autointoxication exists when it is *clinically* evidenced, its occurrence becomes a certainty only, when the intrabiontically formed poisonous material has been demonstrated.

Moreover, the discovery of toxic material in the gastric or intestinal contents or in the feces is no proof that a part of it has been absorbed and has displayed poisonous qualities.

We have seen that the healthy organism possesses certain means of protection against the absorption, transmigration into the blood and retention therein, as such, of enterogenous substances anomalous in quantity as well as in character. Again, synchronous occurrence of intestinal poisons and phenomena of intoxication do not *a priori* evince the latter's dependence upon the former. It must be shown that these poisons were absorbed, that they entered the circulation, that they were transmitted as such to the tissues, and that they were retained therein unaltered and long enough to occasion toxic manifesta-

tions. In other words, these very same poisons, or their derivatives, must be demonstrated in the blood or urine before the autointoxic character of an affection is fully established.

Unsurmountable difficulties often stand in the way of the chemical demonstration of specific substances in the blood. The comparatively small amount of blood obtainable with impunity during the course of a toxic process is one of the factors preventing proper analysis in the vast majority of instances.

In spite of all precautions, withdrawn blood changes very readily; its intravenous injection into another organism is frequently followed by untoward symptoms, no matter whether the blood was derived from a normal or diseased organism. Intravenous injection of the serum of one organism into that of another by destroying the isotony of the blood, or for various other reasons, always acts like a poison. Its behavior in this respect is like that of distilled water, which is always toxic to the corpuscular elements of normal blood. As even normal serum acts as a poison when introduced intravenously into an animal of a different order, it stands to reason, that by injecting sera derived from individuals displaying toxic phenomena, an eventual additional toxicity will be noticeable in the rarest of instances only.

On account of the difficulty of obtaining sufficient or trustworthy results when searching for the autotoxic factors in the blood, their presence was looked for in the urine by a great number of investigators.

It is here that Bouchard's principal labors set in. Not that he was the first to prove the toxicity of normal urine—for this was already demonstrated by Feltz and

Ritter in 1881, by Bocchi in 1882 and Schiffer in 1883—but he was the first to conduct the experiments methodically and on a larger scale, and to adopt a standard from which to calculate the degree of urinary toxicity.

Bouchard's investigations tend to show that normal urinary toxicity is not dependent upon one single specific substance, but upon a number of excretory elements. He claims to have succeeded in dissociating from normal urine, to some degree, seven substances to which he ascribes various qualities. Among these seven substances there are only two which are known to us: carbamid and K. The same observer maintains that the intravenous injection of from 30 Cc to 60 Cc (on the average of 45 Cc) of normal urine for every kilogram of body weight would produce toxicosis; he designates the unit of normal urine which is necessary to kill a kilogram of living matter as "urotoxy," and "urotoxic coefficient" of an individual, the number of urotoxies produced by a kilogram of the same individual in twenty-four hours.

Bouchard's method in determining the degree of urinary toxicity consists in injecting a certain amount of the filtered and neutralized twenty-four hours' urine into the ear vein of a rabbit of known weight. In pathological conditions, the toxic degree of the urine deviates from the normal; it may either decline or increase.

While there is no doubt that intravenous injection into a rabbit of filtered neutralized urine of healthy, and certainly of diseased, individuals, is speedily followed by toxic symptoms like myosis, decline of body temperature, coma and convulsions, there is no parallelism between the degree of urinary toxicity and that of the autotoxic process; that is to say, the toxic qualities of the urine do

not reflect the exact degree of the metabolic disturbances, for the reason that the toxic products may be excreted by other emunctories than the kidney, or that they may become variously transformed during their passage from the blood through the kidney into the urine, in which they may not be contained in the same amount and quality as they existed in the blood. However, besides carbamid and K none of Bouchard's five other toxic elements of normal urine were as yet positively demonstrated. The abnormal, more or less poisonous substance mentioned heretofore, which make their appearance in pathological urines, are almost entirely of non-catabolic origin, and, being the result of putrefactive and dissimilative processes in the intestinal tract, cannot serve as indicators of metabolic disturbances.

Furthermore, the *poisonousness of the renal secretion may depend upon certain elements which do not exist in the blood and which found their way into the urine from another source.* If this is so, and there are a number of substances which may occur in the urine, but never in the blood, as, for instance, indol and skatol, which impart the specific odor to the feces, then I cannot see of what practical value intravenous injections of urine can be in the experimental determination of the autotoxicoses. By means of these injections elements may be transferred into the blood which never occurred therein previously, and thus conditions and phenomena may ensue which are not only anomalous, but which in reality are never displayed by a diseased organism.

Again, although Bouchard contends that the urinary toxicity is not due to the water, but to the substance which it holds in solution, it is an undisputable fact

that a comparatively large amount of fluid, even when it possesses a similar degree of molecular concentration as the blood, intravenously injected, never behaves indifferently toward the organic blood constituents.[1]

The foregoing facts tend to show that the biological test for the determination of urinary toxicity is applicable within very narrow limits; that the intravenous introduction of urine is an inexact experiment for the demonstration of a *specific urinary toxicity;* and that the determination of the urotoxic-coefficient is of very little importance.[2]

There is an additional fact speaking most emphatically against the employment of the biological test in the determination of the degree of urinary toxicity. This fact, it is true, was not known when Bouchard's lectures appeared in print; not until recently has it been taken into due consideration. The urine, namely, does not exhibit the same degree of molecular concentration as the blood; its intravenous injection, therefore, disturbs the isotony of the blood, which is absolutely essential for the proper conduct of the vital functions. The disturbance in the osmotic condition of the blood may become pronounced, to such a degree that all or almost all toxic manifestations may be attributed to it. Physical

[1]It must not be forgotten that the neutralizing salt is by no means an indifferent factor. If the urine is highly acid, so that much alkali has to be added to effect its neutralization, its injection may be followed by more or less pronounced disturbances of the intrasystemic osmotic conditions.

[2]Hymans v. d. Bergh (47) has calculated that in the same animal, according to the fullness or emptiness of the gastrointestinal tract, *i. e.*, according to its absolute weight, the urotoxic coefficient would fluctuate between 0.295 and 0.466.

autointoxication, as I have called the condition arising on the basis of altered intrasystemic osmosis and its consequences, will be treated at greater length when considering the subject of uremia.

However, a certain amount of the toxicity of a urine —the normal as well as the pathological secretion—may be due to a chemical toxicity. The urinary salts of potassium and ammonium exert a toxic activity when they are injected in sufficient amounts.

If urine, in which ammonium carbonate has been developed by fermentation, is injected into the veins of animals, the train of symptoms denoting ammonemia may be produced.

Bouchard maintains that by decolorization of the urine with charcoal it loses about 33 per cent of toxic material. I have approached this point experimentally some years ago and found that decolorization with charcoal usually causes some reduction of urinary toxicity, but certainly not more than about ten per cent, on the average.

Hymans v. d. Bergh (47), on the other hand, observed in his one pertaining experiment that the decolorized urine exhibited a higher degree of toxicity than the unaltered secretion.

The same facts which stamp the biological analysis of normal urine a faulty and unreliable procedure preclude its general employment in urines derived from pathological states. Nevertheless, the determination of relative urinary toxicity may occasionally be resorted to, as I have done in my case of morbid sleepiness, for purposes of general orientation; but far reaching deduc-

tions, definite diagnosis and treatment should never be based upon the findings.

Inasmuch as the biological test has proven a failure, the chemical identification of the poisonous material in the urine seems the only rational method for the determination of the nature of its toxicity. However, the isolation of specific urinary toxic substances by no means implies that they existed as such in the blood. Again, the amount in which urinary substances like acetone, lactic, glycuronic, diacetic and oxybutyric acids are likely to appear in the blood at *one time* is too insignificant to give rise to any noteworthy systemic disturbance. Aside from this fact, the products of the intermediary metabolism—acetone, diacetic and oxybutyric acids—are frequently found in urines of individuals who never exhibited any of the autotoxic phenomena.

Ewald and Jacobson (48) and Albu (49) demonstrated in the urine, during tetany, the presence of diamin compounds which, however, did not prove toxic when injected into animals. Ewald (50) separated (partly by the somewhat modified process of Brieger and partly by Baumann's method) small amounts of alkaloidal bodies (as picrates and double platin salts) from the urines of two cases of Addison's disease, without arriving at any definite conclusion concerning their toxicity.

Ptomains and other bacterial alkaloids isolated from pathological urines, for reasons already set forth, *have no bearing at all upon the genuine autotoxic process.* Their appearance in the urine may stand in some connection with reinfective and, in a certain sense, also with autoinfective disorders. Brieger's and Gautier's far-

reaching discoveries in the domains of the ptomains and leucomains, and the onerous labors of other investigators in the same field, have not contributed towards the understanding of the subject of autointoxication. Alkaloids, more or less toxic in character, were obtained from the urines of many of the infectious diseases. In the urine of measles, glycocyamidin ($NH\ C\ NHCO\ NHCH_3$), a toxic substance, was found. From the renal secretion of individuals affected with influenza a crystalline toxic alkaloid ($C_9H_9NO_4$) imparting pronounced toxicity to the urine, was separated; in whooping cough there may appear in the urine $C_5H_{13}NO_2$, in erysipelas $C_{11}H_{15}NO_3$—bases of proportional toxicity. Pleuritic urine exhibits a crystalline poisonous body, pleuricin ($C_5H_5O_2$); pneumonic urine contains among others an alkaloid of the composition $C_{20}H_{26}N_2O_3$, the amount of which decreases during the period of defervescence. In scarlatinal urine, Griffiths demonstrated the presence of a poisonous, pyretogenic base. All these substances have occurred in amounts sufficient to determine their constitution and physiological activity.

The chemical methods of to-day do not suffice for the isolation from the urine of non-bacterial toxic substances. The methods of Brieger, Baumann and Griffiths do not avail much as far as intrabiontically-produced toxic substances are concerned. Eventual demonstration even of a non-bacterial poison in the urine does not point to its pre-existence in the blood. *Toxicuria is a recognized fact, but whether and to what extent it occurs with, or follows a toxemic state is well nigh impossible to determine with our present means.*

Chapter VII.

THE PHYSICO-AUTOTOXIC STATE AND THE PATHOGENESIS OF UREMIA.

The foregoing remarks make it manifest that in spite of an over-abundancy of literature and the enormous amount of research work devoted to the subject of auto-intoxication, we scarcely possess more knowledge about the chemico-autotoxic factors at the present day than those interested in the subject were cognizant of ten and fifteen years ago. It seems to me that we are laboring in a wrong direction when we try to fasten upon a hypothetical toxalbumin, or upon another unknown toxic substance, every disorder whose origin we cannot otherwise explain. Is it really necessary to assume the existence of specific chemico-toxic bodies in all the so-called autotoxic states?

Singling out normal or abnormal urinary constituents and attributing to their chemico-toxic qualities the causation of certain more or less serious autotoxic disturbances, has never, as yet, led to the proper understanding of a solitary case. It is certainly not my intention to deny the possibility of specific autotoxic factors; I believe that the time will come when we will be better able to isolate them, to trace their proper origin, and to connect a toxiuric condition due to them to a toxemic state of the same foundation. I think, however, that this will be achieved only in comparatively few of the conditions which are now classified among the autotoxicoses. Some of these conditions will be found to depend upon ana-

tomical substrata; the majority of these disturbances, however, will be shown to be the consequence of ectogenous toxic processes.

That it is not a chemico-toxicity which stands at the foundation of all autotoxic states is evinced by the pathology of uremia. The history of the theories of uremia is virtually the history of the evolution of the autotoxic theory. Successively, almost all excrementitious matters, carbamid, tartronyl-cyanamid, ammonia and its carbonate, creatin and creatinin, leucin, urochrom, pigmentary substances, and the potassium salts, alone, or by their concerted operation, have been held responsible for the production of the uremic state.

Abundant evidence, however, has been furnished that none of the retained, known products of metabolism are in themselves toxic to any degree. Ignoring for the present hypothetical toxalbumins and unidentified organic molecules, we find that the most pronounced poisonous qualities are yet divulged by the retained potassium salts. As a matter of fact, their quantity in the serum, even if complete anuria has prevailed for some time, is too insignificant to give rise to the grave manifestations which we designate as uremic. Besides, the symptom-complex of potassium poisoning is not exactly alike to the one of uremia, and, furthermore, there is no conclusive proof at all that the amount of potassium in the ash of uremic blood is invariably increased.

Senator, in his work on renal diseases[51], as regards the etiology of uremia, occupies the same standpoint as did Meissner, Voit, Fleischer, and others before him, namely, that it is not the result of the retention of one specific urinary constituent, but of a number or of all such sub-

stances. Practically the same view is held by Bouchard (l. c.), according to whom uremia is not the consequence of a single toxic principle, but the product of all those retentia which normally enter into the composition of urine.

Strauss[43], the latest exponent of the chemico-toxic theory, who, after the example of v. Koranyi[44], tries to fix the origin of uremia upon retained organic molecules derived from albumin disintegration, opines that his conception of the etiology of uremia is more precise than that of Bouchard. With this I cannot concur, because he was neither able to describe the exact nature of these organic molecules, nor did he offer proof of their supposed specific toxicity; Bouchard and his followers, I think, stand upon a less hypothetic basis when they declare that we do not find in the blood of uremia other factors than those exhibited in the normal state.

The physico-toxic theory of the causation of uremia is based upon the frequently observed fact that there exists an augmentation of the molecular concentration of blood serum in uremia, and upon the additional assumption that this higher concentration is due to accumulation of normal products of retrograde tissue-metamorphosis.

If there occurs no synchronous decline of the general metabolic processes, or if no, or but insufficient, vicariousness is displayed by other emunctories when the excretory activity of the kidneys, the organs paramount in depressing the osmotic tension of the blood, is diminished or totally suspended, the crystalloid substances rapidly accumulate in the serum, causing it to be hyperosmotic. (Stern[45].)

That most instances of uremia are characterized by

augmented molecular concentration of the blood serum is demonstrated by the determination of the latter's freezing-point. The freezing-point of normal blood-sera lies between -0.55° and -0.57° C. A further depression of the freezing-point is indicative of the retention in the blood of abnormal amounts of soluble molecules. In nephritis *without uremic manifestations* the mean freezing-point of the blood, calculated according to the findings of v. Koranyi, Kossler, Lindemann, M. Senator, Rumpel, and Strauss, is situated between -0.58° and -0.59° C. The average freezing-points of the blood in various types of nephritis *with uremia,* calculated from results obtained by aforementioned investigators and by Strubell and Kümmell, lie between -0.61° and -0.67°.

Lindemann[85], who is of the opinion that the increased osmotic pressure of the blood is expressive of the prevailing disturbance in uremia, was the first to maintain that most uremic phenomena could be accounted for by the hyperosmotic condition of the blood.

I had given a somewhat similar interpretation to the various investigations some time before I heard of Lindemann's publication. My first communication upon this subject, entitled "Osmotic Pressure and Its Relation to Uremic Manifestations[86]," was, however, not read until the meeting of the American Medical Association at St. Paul, in June, 1901.

The phenomena occurring in the blood after injections of large amounts of concentrated salt solutions are the same as those in uremia; they make their appearance together with the higher concentration of the blood when the elimination of the accumulated substances from the blood, on account of the resorptive qualities of the tissues, does not occur any longer. (Lindemann, l. c.)

Novi[57] observed tonic and clonic convulsions in dogs after intravenous injection of a ten per cent sodium chlorid solution, in such amounts that the blood possessed twice its former molecular concentration, and he maintains that the origin of these convulsions is due to withdrawal of water from the cortex cerebri, a view, although expressed as early as 1887, practically concurs with the more recent teachings of osmosis.

In a rabbit, weighing 1,320 grams, I have observed convulsive phenomena after intravenous injection of 60 Cc. of a fifteen per cent solution of NaCl. Cryoscopy showed δ -0.72, a marked depression from the normal.

The great number of molecules dissolved in the plasma causing its hyperosmosis, tend to diffuse toward the less concentrated body liquids. During the uremic state, the intercellular liquid in certain tissues may already possess a greater molecular concentration than the serum itself. Ultimately, all the fluids of the body present a similar degree of concentration.

The point of attack and the origin of the uremic convulsive phenomena, according to the experiments of Landois[58], is situated without any doubt in the psychomotor centers of the cortex cerebri. This investigator, who found that extractive substances and salts applied upon the psychomotor centers of the cortex cerebri in dogs give rise to pronounced convulsive attacks resembling minutely the eclamptic or uremic convulsions in men, maintains that the prodromic stage of uremia is formed by the "continuous irritation" of some part of the nervous system by the crystalloids and other excrementitious material in the blood. He does not, however, account satisfactorily for the mode of production of the

"continuous irritation," which, viewed in the light of osmology, may be an expression of the hyperosmotic condition of the blood and liquids in the brain.

Against this etiological conception of uremia it could be maintained, as Strauss (l. c.), for instance, has done, that there are cases in which no analogy had been observed between the degree of molecular concentration and the intensity of the uremic manifestations. While this contention is true enough, there are, on the other hand, very few instances on record in which the freezing-point of the serum was not depressed below -0.58°. Cases of chronic uremia in which the freezing-point of the blood serum was situated between -0.56 and -0.58°, that is, at the normal degree, are not only infrequent, but should be excluded from this consideration, for the reason that they are often spurious (many clinicians too readily designate as uremic any and all nervous phenomena occurring during the course of chronic nephritis), and that the individual attacks are often very slight, which may be indicative of but little altered osmotic condition in the blood plasma or of a quickly passing hyperosmosis.

The not-existing parallelism between the degree of molecular concentration and the intensity of the uremic process could be rather a question of personal equation, as in all other body conditions, than an exceptional or specific phenomenon. While hyperosmosis of the serum is the rule in uremia, Korányi and his followers consider it a concomitant phenomenon and not its etiologic factor. Apart from the few instances in which uremia had terminated lethally when δ had been -0.57° and lower they draw attention to the fact that δ had been found considerably depressed in a variety of disorders in which

uremia had not appeared. Looking, therefore, upon uremia as a chemicotoxic process they assume that the specific poison consists of derivatives of perverse albumin catabolism; that is, of large, almost soluble or insoluble molecules, which, if at all, participate but very slightly in osmotic tension, and do not materially depress the freezing-point.

Among fourteen cases of uremia following the chronic interstitial or the mixed form of nephritis, which came under the observation of Strauss, there were three, viz., one of mild, chronic uremia, one of chronic and one of acute uremia, in which the freezing-points of the respective sera were normal. In the case of mild chronic uremia the amount of retained nitrogen was about twice as large as in the normal; in the two other instances it was excessively increased. Although the more or less depressed freezing-points concurred with an increase of retained nitrogen, in the remaining eleven instances there appeared to be no parallelism between them. For instance, in a case in which δ was -0.68° the retained nitrogen amounted to 266 miligrams in 100 Cc, and in another in which δ was found to be -0.69° the retained nitrogen amounted to 122 milligrams, that is, less than half of the former.

Furthermore, the promulgators of the theory according to which uremia originates from the circulating derivatives of the albumin molecule, like the adherents of the physico-mechanical theory, cannot demonstrate a direct parallelism between the substrata and the resulting phenomena; that is, in this instance, between the amounts of retention nitrogen and the severity of the uremic manifestations.

Accepting, however, augmentation of retained nitrogen in uremia as a proven fact, there is no evidence that an eventual serotoxicity is caused by accumulation of products of normal nitrogenous decomposition alone, or by such of altered albumin-catabolism, or that its eventual poisonousness is of a purely chemical nature.

The albumin molecule is a complex molecule. Being soluble to a very slight degree only, if at all, it does not participate in depressing the freezing-points of the serum or other body liquids in which it is contained. On the contrary, the complex nitrogenous molecule not influencing osmotic tension of the liquid, and representing the principal non-electrolyte of the blood-serum, averts complete dissociation of the electrolytes and thereby further depression of the freezing-point.

The non-electrolytes do not only interfere with dissociation; that is, they do not only limit the number of ions, but also retard their movement. The presence of non-electrolytes, therefore, disturbs and diminishes the conductivity of the electrolytes; that is, the electrical conductivity of the watery liquid in which they are contained.

In uremia the large amount of retained nitrogenous material prevents dissociation of the total electrolytes, and reduces the electrical conductivity of the existing ions. In the concentrated serum of uremia the excess of albuminous retentia increasing the friction of the ions diminishes or prevents their motility. The proportion of nondissociated, neutral molecules to the active, the ions, is excessively large. While the ions as independent molecules, participate in increasing osmotic pressure and in depressing the freezing-point, the excessive high

osmotic tension of uremic serum is not due to its ions, but to its contents of neutral molecules. The ions alone, in the number in which they usually occur in uremic serum, would neither increase its osmotic condition to any extent, nor would they materially depress its freezing-point.

Determination of the freezing-point of uremic blood discloses, therefore, but one fact, namely, that of its high molecular concentration, its hyperosmosis, it does not reveal the presence of excessive amounts of nitrogenous substances, nor is the freezing-point of the serum, *per se,* an indicator of its degree of electrical conductivity.

Dissociation of electrolyte molecules into ions occurs in the ratio of the dilution of the watery solution. The larger the amount of water the more readily ensues this process, the greater the proportionate number of ions and the electrical conductivity. Molecular conductivity is entirely independent of molecular concentration. The greater the amount of the dissolving agent within a certain limit, the greater the conductive properties of a given amount of electrolytes.

In acute uremia, when complete anuria prevails, the dissolving agent occurs in larger absolute amounts; relatively, however—that is, in proportion to the total retained excrementitious substances—it is not increased.

The conductivity of human blood serum increases with its dilution. In other words, the more concentrated the serum, the less its conductive qualities. Uremic serum consequently displays a low degree of electrical conductivity.

Viola[59], investigating the relation of serum dilution to serum conductivity, found the following:

Dilution.	Physiological conductivity (in reciprocal Ohms).
Undiluted serum	111.8
1 Serum plus 1 Water	125.61
1 " " 3 "	141.76
1 " " 7 "	151.06
1 " " 15 "	154.02
1 " " 31 "	162.62
1 " " 63 "	160.98
1 " " 127 "	164.26
1 " " 255 "	158.41
1 " " 511 "	152.57
1 " " 123 "	130.56

The principal non-electrolytes of the blood serum are the albumin substances and their derivatives, of which it contains about 7 per cent; all other nonconductors, such as glucose, lecithin, cholerestin, etc., normally occur in too insignificant quantities to interfere materially with the conductivity of the serum. During the uremic state the nitrogenous products of catabolism in the serum are found to be greatly augmented; the other non-electrolytes are never found increased to such a degree as the albumin derivatives are. In coma diabeticum, on the other hand, it is likely that the hyperglycemic condition stands at the foundation of a diminished electrical conductivity of the serum.

Bugarszky and Tangl[60] found that the addition of one per cent albumin to the blood serum caused an average diminution of 2.5 per cent of the latter's electrical con-

ductivity. (They also demonstrated that about 7 per cent of the serum electrolytes consisted of NaCl, that Na_2HPO_4 does not exceed 3 per cent, and that the remainder consists almost entirely of Na_2CO_3. Thus it evinces that the electrolytes of the blood serum are mostly inorganic salts; the organic salts occur in such small and varying amounts that, normally, they neither diminish nor augment the electrical conductivity of the serum to any extent.)

The experiments of Bugarszky and Tangl leave no doubt that the albumin molecule diminishes the physiological conductivity of the blood serum; being acquainted with the fact that addition of carbamid, for instance, to a solution of NaCl prevents the latter's complete dissociation, we may go a step further and assume that all the complex organic molecules retained in the blood serum occasion a state of diminished electrical conductivity.

Diminished electrical conductivity of the serum seems to be the direct etiological substratum of the uremic attack; the lowest conductivity of human blood yet found, 98.29, was demonstrated in the serum of a case of uremia gravis cum coma (Viola, l. c.). In healthy individuals, the same observer found the conductivitiy of the serum between the extremes 106.18 and 119.*

*Viola mentions also a case of "chronic nephritis with uremia" in which the conductivity of the serum amounted to 125.19. It is not stated whether uremia in this instance was of a chronic nature, which seems most likely. As he designated the other case as "uremia gravis cum coma," we may conclude that in the instance of chronic nephritis with uremia the uremic phenomena were of a mild character.

Infusion of water, or under certain conditions of artificial serum, with or without preceding abstraction of blood, dilutes the serum in such a manner that it may exhibit greater conductive properties. This therapeutic evidence of the reduced conductivity of uremic serum is obtained in a certain proportion of cases only, preeminently in such on the basis of parenchymatous nephritis. In others, therapeutic measures avail nothing whatsoever. A number of reasons may be assigned for this, viz., dilution of the serum may not have been sufficient; albuminous retention may have been present in too large a quantity; normal electrical conductivity may have been suspended for too long a period, or secondary changes may have taken place.

As a general rule, the less retention nitrogen in the serum the greater the chances of reëstablishing its normal conductivitiy by dilution, that is, by enhancing dissociation of the retained molecules. Thus, it seems the uremic phenomena in parenchymatous nephritis can be more readily and frequently subdued than in the interstitial form; one reason, and probably the most formidable, for this is, that in the former the retained nitrogen never, or hardly ever, exists in the enormous amounts in which it is found in the interstitial type.

The occurrence of greater amounts of retention nitrogen in the serum of uremia on the basis of interstitial nephritis will, in a measure, explain its greater "virulence." While the retained nitrogen, without any doubt, reduces the physico-electrical qualities of the serum, and while the co-ordinate and successive manifestations commonly designated as uremic may be accounted for by the diminution or partial suspension of electrical conduc-

tivity in the serum, the accumulated albumin derivatives possibly call forth a secondary intoxication, which may be particularly noticeable when certain uremic sera are intravenously injected into animals. This procedure, however, does not absolutely demonstrate the chemicotoxicity of the uremic blood in the organism whence it is derived. Manipulation of the blood, and may it be conducted under ever so many precautions, always changes its physical condition, and is never without influence upon its chemical nature. Diminished conductivity of the serum is such an inevitable and potent factor in the production of uremic phenomena, that its importance overshadows the eventual occurrence of a secondary toxicosis.

An additional fact was pointed out by Bugarszky and Tangl, namely, that temperature elevation of 1°C. causes an increase of 2.21 per cent in serum conductivity. Recalling that in most instances of uremia, especially in those accompanied by deep and prolonged coma, the body temperature is considerably lowered, we understand again that diminished conductivity of the blood serum stands at the foundation of the uremic syndrome. The influence of temperature upon the degree of electrical conductivity, however, is not only observed in pathological states like uremia, but in all phases and conditions of protoplasmic life. With few exceptions, the higher the temperature the greater the dissociation of electrolytes, the greater again the chemical activity and the evolvement of heat, but if beyond a certain degree, the greater the danger for the continuance of the life of the organism. The lower the intraorganic temperature the smaller, as a rule, the dissociation of electrolytes, the

slower the vital processes. A temperature below a certain degree is inimical to the maintenance or production of a proper conductivity of the fluids of the protoplast or total organism, and consequently to the continuance of vital functions.

Recapitulating the principal points dwelt upon and derived in the foregoing, it is evident that the uremic state arises on the foundation of diminished electrical conductivity of the serum, or at least, that insufficient serum conductivity is a potent contributing factor toward its production.

SUMMARY.

1. None of the retained known products of metabolism are in themselves toxic to any degree.

2. In uremia there is a higher molecular concentration of the blood serum, which is due to the accumulation of normal products of catabolism.

3. Hyperosmosis of uremic serum is evidenced by determination of its freezing-point. The freezing-points of normal blood sera lie between -0.55 and -0.57°C., those of uremic blood sera are depressed to between -0.61 and -0.67°C.

4. In uremic serum there occurs invariably an abnormally large amount of retained nitrogen. There is no parallelism between the degree of freezing-point depression and the amount of retained nitrogen.

5. Non-electrolytes do not only interfere with complete dissociation, that is ionization, but also retard ionic movement. Their presence, therefore, lessens the electrical conductivity of the watery liquid in which the electrolytes are contained.

6. In uremia the large amounts of retained albu-

minous derivatives exhibit most potent non-electrolytic qualities.

7. The ions as independent molecules participate in augmenting osmotic tension and in depressing the freezing-point; the excessive high osmotic pressure of uremic serum is not due to its ions, but to its contents of neutral molecules.

8. Determination of the freezing-point of uremic serum discloses the fact of its high molecular concentration, but not the degree of its electrical conductivity.

9. Dissociation of electrolyte molecules into ions occurs in the ratio of the dilution of the watery solution. The more concentrated the serum the smaller its conductive qualities.

10. The conductivity of the blood serum of healthy individuals varies between 106.18 and 119.12. The lowest conductivity of human blood yet found, 98.29, occurred in a case of uremia.

11. In most instances of uremia, especially in those characterized by deep and prolonged coma, the body temperature is considerably lowered. This fact again contributes toward reduction of serum conductivity. Elevation of temperature, on the other hand, as long as within well-defined limits, tends to increase the conductivity.

The clinical and other data of the case of morbid sleepiness which I set forth when speaking of the neuroses on the supposed basis of enterogenous autointoxication, in a measure tend to confirm the possibilty of a physico-electrical substratum of pathological states which are considered the expression of chemico-autotoxic pro-

cesses. Like Furet, I interpreted narcolepsy as an autotoxic manifestation until I undertook the study of the case in question. However, as not a single symptom pointing to any of the pertaining and known types of autointoxication could be detected, we have to conclude that there stands no autointoxication, at least none in the sense in which we commonly accept the term, at the foundation of this particular case of morbid somnolence.

The conclusion, moreover, is substantiated by the fact that the physical condition of the patient, besides the repeatedly mentioned anomalies, in no respect leaves anything to be desired.

It follows by no means that the primary cause of this instance of pathological sleep is necessarily also the underlying factor in the production of any or all other cases of morbid somnolence. There is no doubt that many ectogenous as well as endogenous intoxications are inducers of abnormal sleep, and of sleeping seizures. There must, however, exist a class of cases closely related to the one described which, while we cannot designate them as idiopathic, are certainly not attributable to any of the known intoxications.

While the urine exhibited less toxicity than is generally possessed by normal urine, and while it did not contain any abnormal substance, it served as the excretory means of an unusually large amount of chlorin (facts which would point to the retention in the blood of toxic elements if the clinical course of the attacks would not contradict this).

The urinary chlorids represent the greater part of the chlorids derived from food and drink. A portion of the ingested chlorin, however, in the form of sodium

chlorid, is contained in sweat, tears, saliva and feces. The patient in twenty-four hours egested about as much chlorin in his urine as he had ingested with his seven liters of milk. In calculating the milk-chlorin I have made use of Bunge's[21] figures, but naturally the composition of the best milk varies within certain limits. If we now consider that the individual is afflicted with hyperchlorhydria—a condition in which, analagous to the normal state, the chlorin virtually occurs ecto-organically, and that he perspires more or less all the time, but very profusely prior to a narcoleptic seizure—we are forced to accept that for certain periods during the twenty-four hours the output of chlorids exceeds the supply, and that there exists a temporary deficit of chlorids in the blood.

In a certain respect this is a condition contrary to the one prevalent in acute febrile states and in many chronic disorders. This fact is readily understood when we recall that fever itself is nothing but an indication of accelerated or more intense vital processes, and that many chronic diseases are nothing else but the result of accelerated or otherwise perverted functions. The acceleration or greater intensity of any vital process, however, is dependent upon a corresponding increase of the osmotic tension. The moment the latter begins to decline, the reactive stage of the fever sets in. Large amounts of chlorids then leave the organism by the kidneys and sweat glands, and catabolism again approaches its normal degree.

Arising from the deficiency of chlorids in the blood, there exists a relatively low osmotic pressure; as a consequence of the decreased osmotic tension we find, for

the time being, diminished nutrition or stimulation of the nerve substance, and therefore interference with its electrical conductivity. The sudden seizures of somnolence are explainable by the lowered nerve impulses conducted through the cells of the central system.

Diminution of osmotic tension, as it apparently prevails during the narcoleptic state, is by no means identical with an anemic condition of the central nervous system during that period; the contrary seems to be the case, that is, we have a hyperemia of the brain, as we very likely find it during the physiological sleep, and coincident therewith we meet with a lowered degree of osmotic pressure.

Neither undersupply nor oversupply of blood, as such, appears to exert any influence upon the production of sleep seizures. These seem to be due, in the first instance, to diminished ionization of the chlorids in the blood—at least so in the case recorded. Other instances of pathological sleep may primarily depend upon the nondissociation of other salts. The chlorids, however, appear to play a very important rôle in the osmotic tension and the electrical conductivity of the body fluids, and their excessive diminution or nonionization may call forth various other abnormal conditions commonly looked upon as chemico-autotoxic in origin.

Chapter VIII.

RECAPITULATIONS AND CONCLUSIONS.

In the foregoing pages it has been shown:

1. That autointoxication as the cause and complication of disease is not a conception of recent origin.

2. That the term "autintoxication" implies self-poisoning of the organism by the retention of excessive amounts of normal, or by abnormal products of its own digestive or metabolic processes.

3. That the autintoxication is "intestinal" when its supposed causative factors have arisen within the digestive apparatus, that it is "catabolic" when it is of apparent intra- or intercellular origin.

4. That toxic phenomena due to ectogenous material cannot be considered autotoxic in character and that the bacterial toxins, even when of enterogenous formation, are not true intrabiontic substances.

5. That "infection" and "autoinfection," and the toxic substances yielded by food-stuffs cause toxicoses but not autotoxicoses.

6. That enterogenous autotoxicosis presupposes the participation of the cellular energy of the gastrointestinal mucosa in the production of the toxic factor.

7. That the organism possesses various means of autoprotection against enterogenous poisons.

8. That typical cases of enterogenous autotoxicosis exhibit a more or less characteristic snydrome.

9. That intestinal autointoxication (and alimentary toxicosis) is not depending so much on the admission to,

as on the retention in, the blood of incompletely converted material.

10. That a differential diagnosis between enterogenous autotoxicosis and ectogenous toxicosis or infection, when the clinical pictures alone are considered, can frequently not be attempted.

11. That the pathological substratum of a "chronic form of intestinal autointoxication," enunciating itself in an enduring clinical picture and presupposing an uninterrupted production of a specific poisonous material, will always remain undemonstrable to a certain degree.

12. That various diseases and complications whose causes have been assigned to intestinal poisons have NOT *been proved to be the consequence of the latter; their nonintrabiontic production, however, is equally difficult of demonstration.*

13. That catabolic autointoxication comprises all processes which are the supposed direct or mediate result of retained and accumulated, of incompletely or perversely converted, or unattenuated, or nondissociated, or irregularly-combined substances, derived from beyond the stage of anabolism.

14. That, unlike the intestinal poisons, there prevails no uncertainty as to the intrabiontic origin of the causative factors in catabolic autointoxication.

15. That catabolic autointoxication may result from autolysis, acidosis, nucleolysis, anomalous "internal secretions" and the retention of normal substances causing disturbance of the osmotic conditions in the blood.

16. That the autotoxic condition arising on the basis of "acid intoxication" is not due to a specific toxicity of the acids, but to faulty alkali supply.

17. That the alkali does not reach the blood current at all, or that it passes in and through the blood without entering the cellular structure in which the acid formation has ensued.

18. That the toxicity of uric acid is still an unproven factor, but that the xanthin bases display toxic properties.

19. That the amount of uric acid may serve as a general indicator of the intensity of the nucleolytic processes, but that it is not always the principal product of nucleolysis.

20. That some diseases and disturbances may occur secondary to augmented nucleolysis, but that they are not secondary to the nucleolytic products.

21. That almost all hypotheses and assumptions pertaining to the relation of the "internal secretions" to autotoxic manifestations still await experimental confirmation.

22. That in a certain sense most catabolic autotoxicoses are to some degree retention autointoxications.

23. That the retention of excretory products is due to the insufficiency of the various organs of elimination, mainly the kidneys.

24. That a pronounced specific chemico-toxicity of the retained substances was not proven in a single instance.

25. That we may accept a "physical autointoxication" as the consequence of the retention in the blood of normal products of dissimilation.

26. That a number of autotoxic states are explainable on the basis of the altered physical conditions in the body-fluids.

27. That the anomalous osmotic conditions in the blood are often associated with the impaired electrical conductivity of the serum.

28. That the narcoleptic, and some forms of the epileptic, attack, stupor and the terminal coma of carcinoma, diabetes mellitus and uremia (notwithstanding the discrepant manifestations of the various comatose states) are expressions of the diministed electrical conductivity of the blood-serum.

Part II.

THERAPY OF THE AUTINTOXICATIONS.

Chaptve IX.

TREATMENT OF INTESTINAL AUTINTOXICATION.

1. General Considerations.

We have seen in the foregoing that a positive diagnosis of enterogenous autointoxication can be but rarely established. Most cases of supposed intestinal autointoxication are in reality ectogenous toxicoses. But, fortunately, notwithstanding their discrepant etiology, the general treatment of intestinal intoxication, as far as it goes, is in many respects so much like that of intestinal autotoxicosis that the question whether we have to deal with a simple toxicosis or an autotoxicosis, in a given instance may frequently be of academic interest only.

While the treatment of ectogenous intestinal poisoning confines itself to the removal or the neutralization of the already existing toxic substances, a rational therapy of intestinal autointoxication should be designed to avert also the new and continued formation of the *materia peccans.*

Although the management of a case of intestinal autointoxication should primarily be directed towards the removal of the cause, symptomatic and even prophylactic treatment must be resorted to in most instances. The symptomatic treatment shall assist and restore impaired functional activity—the indications for its institution are the same as in cases of ectogenous poisoning. Preventive measures have their special field of usefulness in individuals in whom autotoxic phenomena have super-

vened repeatedly, or in whom an autotoxic state of apparent chronicity has established itself. Whenever faulty elimination seems to have been at the bottom of the autotoxic process, prophylactic treatment to stimulate the emunctories and to aid the work of excretion should be instituted as a matter of course. By such means autotoxicosis may be prevented altogether, or, if not entirely suppressed, its course will at least be mitigated.

The etiological treatment of intestinal autointoxication would be comparatively simple if the poisonous substances remained at their seat of formation. This, however, is not the case. The toxic phenomena are the result of the absorption of the poisonous material; were the latter to abide in the enterium to be excreted with the feces in due time, autointoxication would not ensue. The exhibition of autointoxic symptoms, hence, is evidence of the complete or partial absorption and the retention in the blood and tissues of the enterotoxins. Thus it is evident that removal of gastric and intestinal contents alone, as Senator[1] still recommends, does not suffice to cure an attack of autotoxicosis. Such removal may prevent further absorption for the time being, but it does not eliminate that part of the toxic material which has already entered the circulation.

The same may be said of agents introduced for the purpose of neutralizing the poisonous qualities of the gastro-intestinal contents. As long as the toxic substances remain in the alimentary canal they may be influenced by therapeutic, if but empiric, measures; the very moment they are taken up by the blood current—and then only their toxic properties are displayed—the antidotes are useless in combating the actual toxicosis.

The etiological treatment of intestinal autotoxicosis must, therefore, be extended to the lymph, blood and tissues. In as far as the nature of the enterogenous poisons is hardly ever known, specific neutralizing substances to act in the blood cannot be introduced. Agents employed for this purpose are used empirically. The treatment to be immediately instituted in a case of intestinal autointoxication, besides evacuation of the gastro-intestinal canal or neutralization of its contents, consequently limits itself to stimulating lymph metabolism and augmenting or accelerating the processes of elimination.

2. Evacuation of the Gastro-Intestinal Canal.

The stomach is not often the seat of the production of intrabiontic poisons. The elimination of the causative factors of enterogenous poisoning from the stomach by inducing vomiting or by gastric irrigation and lavage is, therefore, well-nigh impossible. On the other hand, these measures may be employed to advantage whenever, after the toxic manifestations having first declined, they recur in augmented degree. The recurrent toxic symptoms—if the intestinal tract has been carefully freed from its contents—may be caused by the reabsorption of the poisons which had been excreted into the stomach. We know that a number of poisons may be secerned into this organ from which they may eventually become reabsorbed. Among the poisons which find their way from the blood into the stomach there are some alkaloids and fatty acids and snake venom, in short, substances between which and the enterotoxins there may be direct or more remote points of analogy. While the employment of gastric irrigation and lavage may thus prevent re-

absorption of the autotoxic material, they will never be of any such importance in the treatment of autointoxication as they are in the management of certain cases of ectogenous poisoning.

When removal of the gastric contents is contemplated lavage of the stomach should always be given preference over emesis. Lavage should be employed, particularly, when reabsorption is threatened, that is, in such cases in which the morbid phenomena have been exhibited already, in which, in other words, the organism is greatly weakened, the resistance diminished and the circulation impaired. Forcible ejection of the gastric contents, induced by emetics, may not only bring on collapse of a patient already reduced in vitality, but it never causes as complete an evacution of the stomach as may be produced by irrigation or lavage. If, however, emetics are resorted to, either because no stomach tube is available or because its introduction is impossible, one should abstain from employing fatty substances, in which many poisonous bodies are readily soluble, or from administering warm water, which stimulates the gastric mucosa and thus facilitates absorption of the material contained in the organ.

The best emetics in such cases are apomorphin hydrochlorate, 0.004—0.0065 Gm. (1/15—1/10 gr.), hypodermically, to be repeated every 15 minutes till effective; pulverized mustard, 10 to 15 Gm. in 60 to 200 Cc. water (dr. 2½ to dr. 4 in fl.oz. 2 to 7); zinc sulphate, 0.6 to 2 Gm., in 30 Cc. water (10 to 30 gr. in fl.oz. 1); and copper sulphate, 0.12 to 1 Gm. (2 to 15 gr.).

Inasmuch as the intestines are the probable place of formation of the *causa morbi* of the type of autotoxicosis

under consideration—at least they are the organs whence absorption of poisonous material lodged within them takes place—their evacuation should be accomplished with great dispatch. It matters not whether we have to deal in a given instance with an intestinal toxicosis or autotoxicosis—the removal of the intestinal contents is essential in both eventualities. Best suited for this purpose are the saline purgatives which, with their respective maximum doses, are enumerated in the following:

Magnesium citrate, 10 Gm. (oz. 2½).
Magnesium sulphate, 30 Gm. (oz. 1).
Potassium bitartrate, 60 Gm. (oz. 2).
Potassium tartrate, 15 Gm. (oz. ½).
Potassium and sodium tartrate, 60 Gm. (oz. 2).
Sodium phosphate, 30 Gm. (oz. 1).
Sodium pyrophosphate, 15 Gm. (oz. ½).
Sodium sulphate, 30 Gm. (oz. 1).
Sodium tartrate, 30 Gm. (oz. 1).

The maximum dose may be repeated once or twice. In large doses these salines do not only augment intestinal peristalsis, but also the enteric secretion. If in the presence of a fairly emptied enterium a succession of autotoxic attacks, of which each succeeding one is milder, takes place, that is, if a portion of the materia peccans remains in the tissues, lymph and blood, these salines should be administered in doses small enough to increase systemic metabolism and excite diuresis. The saline purgatives, given in amounts somewhat less than their minimum laxative dose, from three to eight times during the twenty-four hours, are excellent stimulants of metabolism and promoters of elimination.

Purgatives and drastics of an oily nature are, on ac-

count of their toxin-solving qualities, not so well adapted in cases of poisoning originating in the intestinal tract as are the salines. However, if the amount of castor oil administered at one time is large enough to effect complete evacuation of the bowels within a short time, undue results will not accrue from its use. At any rate, oily purgatives should be resorted to only when salines are not at hand. Cholagogues, as well as remedies like cascara sagrada, aloes and colocynth, whose specific field of action is the lower portion of the colon, are useless for the purpose in question.

The majority of instances of supposed toxicosis take their origin in the small intestines. Their contents can be removed only by purging. Enemata and enteroclysis hardly ever display direct activity outside of rectum and colon. Yet, they have a distinct place in the local treatment of autotoxic processes—the removal of disintegrating masses of mucus from the large bowel, the relief of colic and of other distressing symptoms, the breaking up of fecal impactions and the clearing of the lower bowels.

Indirectly, it is true, enteroclysmic applications occasionally may induce evacuation of the small intestines. The direct effect of enterocylsis on the small intestines, however, is so uncertain that one could not rely upon it to empty the intestines during an attack of poisoning.

The high enema is given through a colon tube or a soft catheter of large lumen. Care must be taken that the tube does not bend on itself when a large portion of it has passed into the rectum. The patient should be in the dorsal position with hips elevated. If large amounts are to be injected so that the colon may be completely filled at one time, the patient should lie first on his left

side; after introduction of from 500 to 750 Cc. he should occupy the dorsal position, and when another 500 Cc. have been injected he should rest on his right side.

The temperature of the enema should be a few degrees above that of the body. The mean amount of fluid administered by high enema should be:

For infants, 25 to 50 Cc.; for a child 2-6 years, 75 to 150 Cc.; for a child 6-12 years, 200 to 500 Cc.; for adolescents 12-18 years, 600 to 1,000 Cc.; for adults, 1,000 to 1,500 Cc.

Soap suds answer best for the removal of mucus and fecal impaction. Sweet oil, or olive oil, may be added up to 5 Cc. to every 100 Cc. of the injection fluid. Addition of from gtt. V to gtt. X of oil of turpentine to every 100 Cc. of the enema enhances its stimulating action, and hence is particularly useful in cases of intestinal poisoning. At the same time, the turpentine relieves eventual flatulence and colicky pains. The following combinations, administered as high enemata, insure rapid unloading of the colon:

℞ Ext. Colocynthidis .....2 Gm., or dr. ½
Saponis mollis.....4 Gm., or dr. 1
Aquæ .....500 Cc., or oz. 16

℞ Tinct. Aloes.....12 Cc., or fl. dr. 3
Olei Olivæ.....100 Cc., or fl. oz. 3
In 1,000 Cc. (℥XXXII) of soap suds.

Enteroclysis, with the single as well as with the double current, may be employed instead of the high enema. It will be found, however, that the enema is more serviceable to quickly cleanse the colon of its contents, and that the continuous irrigation of the bowels is best practiced

after the larger fecal masses have made their escape. The irrigation with warm salt solution is continued until the fluid returns clear. It is especially indicated for the purpose of promoting the general metabolic processes by which the enterotoxins are eliminated from the organism.

3. Neutralization of Gastro-Intestinal Poisons.

In cases of poisoning by a known substance it is easy enough to select a chemical or physiological antidote for the residual poison remaining in the stomach or the intestinal tract. If, on the other hand, the poison is unknown, and if it does not give rise to distinct symptoms by which its exact nature is revealed, rational antidoting can, of course, not be attempted. In poisoning by tainted food, in supposed ptomain poisoning and in other forms of intestinal toxicosis of practically unknown origin, antiseptics are simply mixed with the residual intestinal contents. These antiseptics are given in accordance with the hypothesis that all toxic processes are the result of bacterial interference, and that they destroy or inhibit the growth of the pathogenic intestinal micro-organisms.

Aside from the fact that complete intestinal asepsis is neither possible nor even desirable, the administration of disinfectants in acute intestinal poisoning, regardless of their dose, their toxic and corrosive effects, of the character and amount of associated material, and regardless of the type of micro-organism and the number eo be made innocuous, to say the least, is extremely irrational. If the haphazard employment of antiseptics in intestinal poisoning is an unscientific procedure, how much more empirical must be the administration of anti-

dotes, so-called, in an autointoxication of whose underlying factors we possess not the slightest intimation!

Hence, it is obvious that we cannot speak of a rational neutralization of the materia peccans in enterogenous toxicoses. Indeed, the employment of the various agents to render intestinal poisons innocuous, although frequently producing the desired effect, is almost entirely dictated by empiricism alone.

The stomach and colon are readily emptied of their contents by lavage and irrigation. In these parts of the alimentary tract antidoting is, therefore, called for but rarely. The field *par excellence* for neutralizing drugs is the small intestines which are out of reach of the stomach tube and of enteroclysis. Neutralization of the poisonous material lodged in the small intestines can only be effected, if at all, by administering the antidote *per os*. If unconsciousness prevails and if swallowing is interfered with, attempts at neutralization should be abandoned entirely, or should be postponed until a more opportune time.

Calomel deserves first rank as a neutralizer of enterotoxins. Whether its action is a direct one, or whether it stimulates the liver to perform its sentinel duties, or whether its effect is exerted upon the excretory glands in the lower part of the small intestines, thereby giving rise to the neutralizing secretions, cannot be decided with our present knowledge. Apart from keeping up the peristalsis by which the intestines are held empty, calomel in doses of from 0.006 to 0.06 Gm. (1-10—1 gr.), repeated every 15 to 30 minutes, is an excellent promoter of diuresis. The administration in small doses should be continued for from 18 to 48 hours.

Sodium sulphide (Na^2S+9H^2O), possesses effective general antidotal properties. I first tried this drug in a case characterized by chills, dyspnea, reflex vomiting, oliguria and somnolence, in which all measures employed had failed to bring about decided amelioration of the condition. I had used sodium sulphide with very gratifying results a few days previously in a case of acute lead poisoning, and was thus prompted to employ it in the case of autointoxication after the other agents had proved useless. I have since administered the drug in a number of instances of intestinal toxicosis and autotoxicosis, in which it has almost always shown its efficacy. I give it in doses of 0.06 Gm. (1 gr.), from five to ten times a day, in plenty of water, immediately after application of the high enema. Evacuation of the stomach, when necessary, must be accomplished before pursuing with the administration of the drug. It is best to continue the drug for four or six days.

Another substance of distinct antidotal value in toxic processes originating in the intestines is formic acid. It may be taken before or after removal of the gastric and colonic contents, in doses of gtt. 2 to 5, well diluted, every hour. A few drops of glycerin may be added to cover the taste. Besides its pronounced antiseptic qualities, which it has no occasion to exhibit in genuine intrabionitic toxicosis, formic acid undoubtedly exerts a specific influence upon the enteric secretion. Sodium formate and the other formates do not seem to possess this property.

Brewers' yeast occasionally displays remarkable antidotal characteristics. At other times it behaves indifferently, or even causes oppression, meteorism and

dyspnea. The action of yeast in intestinal disorders has been variously explained. It has been ascribed to its influence upon the intestinal parasites, to its nuclein and to its ability to convert the carbohydrates in the small intestines. Parasites and carbohydrates are possible factorc of ectogenous intoxication, but have no bearing upon autointoxication proper, and the nuclein is not a neutralizing factor. In my opinion, there is no question that the specific action of yeast in diversse pathological conditions of the intestines is due solely to its *zymase*. This exerts either a specific influence upon the poisonous substances contained in the small intestines, converting them into innocuous material, or it supplies a deficiency in the enteric juice, thereby inhibiting the toxic action of these substances, or their continued production, or both.

The indifferent or untoward effects of yeast in therapeutics are frequently due to the utilization of the ordinary impure yeast, that is a mixture of different species contaminated with large amounts of bacteria. In order to obtain satisfactory results it is absolutely necessary to employ pure culture yeast, that is yeast derived from one single cell.[a] Dried yeast, as long as it is a pure culture product and uncontaminated, which latter, by the way, is very difficult to obtain, may be employed instead of the liquid form, but it must not be forgotten that the drying process reduces yeast activity. Hence, dried yeast must be administered in somewhat larger doses. The dose best adapted for the treatment of toxic states arising from intestinal poisons is from 20 to 40 Cc. of the liquid, and from one to two teaspoonfuls of the dry product. Yeast must not be given

together with antiseptics, as these interfere with yeast activity. In suitable cases its administration may be continued for protracted periods.*

In the foregoing I have briefly dwelt upon four neutralizing agents, representing four different groups of medicines. Excepting formic acid, none of these drugs displays any marked antiseptic qualities. Formic acid itself has been mentioned on account of qualities other than disinfectant. Antiseptics as such have no place in the treatment of genuine intrabiontic poisoning.

4. Stimulation of Lymph Metabolism.

We know that certain substances introduced into the blood are apt to remain in the lymph in greater proportion, and for a longer period, than in the blood. If anything is to be inferred from this fact, it is the probability of the comparative slowness of lymph metabolism. Furthermore, it may be concluded—and everything points to this probability—that the bulk of the absorbed intrabiontic poisons is deposited in the lymph for the time being. To stimulate lymph metabolism, that is, to increase the flow of lymph, is, therefore, a rational, and as the results show, a beneficial procedure in cases of autotoxicosis.

The best remedies for this purpose are undoubtedly some of those which Heidenhain has designated as "lymphagogues of the second class." Such lymphagogues are sodium chloride and other neutral salts. In-

*Lupuline, which I found to be a very valuable agent in the treatment of many disorders taking their origin in the intestinal canal, possesses little virtue in neutralizing autotoxic processes. Its real value is exhibited in diseases due to intestinal *infection*.

travenous injection of hypertonic solutions of these crystalline bodies, causing augmented osmosis of the blood, is followed by the transmission of water from lymph and tissues into the blood. Increase of tension in the capillaries, which is proportional to the increase in the volume of the blood, is the further result. The higher capillary pressure gives rise to a much augmented transudation of fluid from the capillaries, and hence in the lymph-flow from the thoracic duct.[68]

The action of saline lymphagogues depends upon their direct injection into the blood current. The administration of the solutions by hypodermoclysis is, as a general rule, not followed by a markedly increased lymph flow. Intravenous infusion is accomplished much more readily by venepuncture than by venesection. I use for this purpose a venepuncture needle of my own design fully described elsewhere. The technique and details pertaining to venepuncture will be considered later.

Sodium chloride, always quickly obtainable, if properly employed is as good a lympagogue as any. The strength in which NaCl is commonly injected by venous infusion or hypodermoclysis is the decinormal, that is 0.6 per cent solution. Such a solution, however, is hypotonic. Isotonic with human blood is a solution of NaCl of 0.91 per cent. A hypertonic solution, such as will cause increase of lymph flow, must contain more than 0.91 per cent of the salt. A solution of one per cent suffices for all practical purposes. It should be given in amounts up to 500 Cc., at a temperature of about 46°C (115°F). It may be repeated every four to six hours if the autotoxic phenomena do not abate.

5. AUGMENTATION AND ACCELERATION OF THE PROCESSES OF ELIMINATION.

All treatment of intestinal autointoxication, besides the direct antidoting of the enterotoxins, is aimed at the improvement of the eliminating functions. The means which are advocated as evacuants of the intestinal tract, the saline lymphagogues and even some of the antidotal agents, act as efficient eliminants, especially as diuretics, if employed in the proper manner. There is no more simple nor better method of producing diuresis at our disposal than enteroclysis of large amounts, from 4-8 litres of 0.6 per cent sodium chlorid solution. Hypodermoclysis or intravenous injection of this or a more concentrated NaCl solution, gives rise to similar diuretic effects. In cases of enterogenous toxicosis, during the prevalence of the acute phenomena, it often is impossible to administer remedies *per os* while enteroclysis may be performed in practically every instance. Elimination of the toxic substances from the blood into the intestines may be brought about by salines taken *per os,* or by their enteroclysmic introduction. This method is particularly adapted for the treatment of certain forms of metabolic autotoxicoses and will be dwelt upon elsewhere.

By stimulating the sweat secretion, a portion of the poisonous material may be eliminated through the skin. The perspiration, in order to be of immediate benefit, should be very profuse and should be induced by steam or dry heat. Diaphoretics, tending to produce cardiac exhaustion, have no place in the management of the autotoxic state.

The possible relief of the toxic condition afforded by stimulating salivary secretion is too insignificant to receive more than mention on this occasion. Sialagogues, as such, are without a specific field of application during the acute stage of intestinal toxicosis.

Chapter X.

TREATMENT OF INTESTINAL AUTINTOXICATION (CONT'D).

SPECIAL THERAPEUTICS OF PATHOLOGICAL CONDITIONS OF SUPPOSED ENTERO-AUTOXIC ORIGIN.

Special Therapeutics—Before entering upon a therapeutic discourse of the various affections usually ascribed to intestinal self-poisoning, we should understand the following points.

a. The diverse pathological states hereafter enumerated are frequently expressions of simple toxicoses.

b. These toxicoses are mostly enterogenous; their autotoxic origin, although plausible and clinically evident, lacks positive demonstration in almost every instance.

c. In recurrent attacks, discriminating diagnosis between simple enterogenous toxicosis and autoxicosis must be attempted.

d. Irrespective of the ectogenous or intrabiontic formation of the *materia peccans,* the general treatment of all acute toxicoses is the same, as a rule.

e. Inasmuch as entero-toxicosis and entero-autotoxicosis cannot be readily discriminated at the beginning or the height of an attack, and inasmuch as the food is frequently an element in the causation of the former, it is best—when confronted with a toxic state—to withhold all nourishment, except water, for the time being, until the acute toxic symptoms have abated.

f. Removal or neutralization of the cause does not always obliterate the pathological effects; the *materies morbi* may be but stimulators of anomalous activity and promoters of toxic states, the latter, however, may endure considerably longer than the factors that stand at their foundation.

g. Morbid phenomena ushered in by an intestinal crisis or autotoxicosis, when attaining a certain degree of chronicity are not any longer symptomatic of the toxic process and must not be treated as such.

h. Acute toxic manifestations, in addition to the etiological therapy should, if necessary, be treated symptomatically.

DERMATOSES.

Enterotoxic skin affections may be occasioned by,

a. The action of enterotoxins upon the peripheral nerves and in the capillaries.

b. The action of normal but excessively produced enteroproducts upon the peripheral nerves and in the capillaries.

c. The excessive vicarious action of the skin when other excretory organs are diseased.

d. The insufficiency of the tegumentary emunctories in eliminating enteroproducts normal in amount and quality.

Hyperglycemia and the Resulting Dermatoses.

The diabetic state in as far as it is not the result of a general bodily deterioration may be looked upon as an enterogenous intoxication. It is not an autointoxication in the sense in which I have defined the latter as its production is due to a *materia peccans,* partly preformed in the ingesta, partly readily elaborated from them. How-

ever, the incomplete conversion and the subsequent absorption of large amounts of glucose (the enterotoxin in these instances)—pointing to an insufficiency of some organ—to a certain degree justifies the assumption that hyperglycemia is an autotoxic condition.

Objects to be attained: Reduction to the physiological amount of glucose in blood, lymph and tissues; enhancement of the glycolytic functions.

Etiological treatment: Withdrawal of saccharine and sugar-forming ingesta; prevention of glucose absorption by increasing intestinal peristalsis; augmentation of oxidation processes by moderate exercise, lung gymnastics, air or water baths, hot air, friction.

Symptomatic treatment: Application of antiseptics to the lesion to prevent bacterial invasion; emollients; local sedatives or stimulants according to indications.

Preventive treatment: Continuance of dietary regulations—more or less modified—for protracted periods; continuance of other etiological measures.

Other Dermatoses.

Urticaria, erythema, acne, pemphigus, impetigo and a number of other skin affections are frequently the result of gastro-intestinal crises. Therapeutic proof substantiates this etiological conception in many instances.

Objects to be obtained: Amelioration of gastro-intestinal disturbance; prevention of subsequent paroxysms; dispersion of local affection.

Etiological treatment: Evacuation of stomach and intestines; continued irrigation of colon; salines in full doses. Neutralization of intestinal contents with sodium sulphide; yeast, by os or by rectal administration, in the latter case a tablespoonful of an active desiccated

preparation in 150 Cc water of 37.7°C (100°F) at bedtime. The injection is to be retained.

Symptomatic treatment: Any application containing a sedative; bland dusting powder or ointment, atropin in doses of 0.001 Gm (1-60 gr.) twice daily, its effects to be closely observed.

Preventive treatment: Discontinuance of certain foodstuffs and habits; aperient mineral waters for some time; occasionally administration of calomel.

NEUROSES.

The direct connection between apparent disease-entities involving the nervous system or the brain and intestinal autintoxication has not been definitely established in a single instance. Some such affections are expressions of simple intestinal toxicoses and should be treated accordingly. Others may be the result of anomalous metabolic processes. Intestinal autointoxication, as pointed out before, may be one of the elements in the production of certain nervous and mental disorders; it may furnish the exciting agent but it is not their sole causative factor.*

The toxic material may occasion neuroses by:

a. Production of motor paralysis.
b. Production of motor irritation.
c. Diminution of electrical conductivity.
d. Alterations in the nerve substance.

*Neurasthenia and other nervous affections which have been associated with enterotoxemia seem rather complications of chronic gastro-intestinal disorders than the results of specific enterotoxins. The principles of general autotoxic treatment should not be applied to the diverse affections underlying neurasthenia, meningoform disturbances, acute ascending paralysis, etc.

Epilepsy and Epileptiform Disorders.

That epileptic or epileptiform seizures may be the consequence of the ingestion of certain substances is a well-authenticated fact. Magnan[54] found that "absinthe" frequently promotes epileptic symptoms. That the excessive use of alcoholicis may be followed by epileptic seizures has long since been recognized. For details as to epilepsia alkoholica I refer to my article on the subject.[55] In this form of epilepsy acetone or diacetic acid may be the mediate precursor or a concomitant of the toxic state.† If these substances are directly evolved

†This contention is based upon the following case of mine, the complete history of which will be found in above mentioned contribution[55].

Patient, a woman, 45 years old, mother of eight children who were all alive, was first seen by me on June 1, 1895. Personal and family history good. Patient was under the influence of whiskey, the first dose of which she had taken two days previously. She complained of "sour stomach and sick headache." Towards evening of the same day I was summoned again. I found her then in a state of somnolence. I was told that she had had a "fit of twitchings all over her body." Soon after she awoke and regained consciousness, but within a few minutes she had a second attack which was undoubtedly of an epileptic nature. During the night she had two similar seizures. The occurrence of previous epileptic paroxysms was absolutely denied by the family and by the patient herself. The following day she felt quite comfortable. On June 2 and 4 acetone and diacetic acid were demonstrated in the urine; on the 6th these substances were not any longer exhibited.

Patient discontinued the use of alcohol until the middle of March, 1896, when she indulged freely again. On the 18th of that month she had an epileptic seizure similar to those which occurred during the previous June. On March 20, 24 and 25 the attacks recurred. On the latter day I observed some char-

from the ingested alcohol the intoxication is of an ectogenous character; if the acetone bodies are occasioned by the action of the alcohol on the body-material, or by the insufficiency of a certain intrabiontic function, the convulsive disorder with a moderate degree of justification may be looked upon as autotoxic in nature.

Toxic epilepsy of whatever specific origin, should be treated on general antitoxic principles. After removal

---

acteristic features of alcoholism, there being tremor and trembling of the tongue, great impairment of the appetite and digestion and obstinate constipation. Amnesia, semiunconsciousness, hallucinations, great fear and a suicidal tendency, which were reported to me, convinced me that her state was one of melancholia alkoholica. The hallucinations continued and were of a religious character. This condition lasted for about two weeks, during which time she refused all nourishment but milk. The urinalysis showed acetone and diacetic acid. From July 16 to July 26 the epileptic seizures recurred at intervals, the tremor, incoherent language, melancholia and defective memory continuing. During the night of September 5th I was summoned to the patient and found her lying on the floor breathing heavily. She was unconscious. Her eyes were staring and wide open. From then until her death she was mostly unconscious. During a fortnight a quasi-continuous convulsive epileptic condition prevailed, the patient having as many as fifteen daily seizures. Repeated urinalyses revealed the presence of acetone and diacetic acid; glucose or albumin could never be demonstrated. After having been in a profoundly comatose state she finally died on October 6. The family did not permit an autopsy. As for most of the time the patient was subsisting on milk alone, there can be little doubt that the acetone and diacetic acid were derived from the alcohol or from the body substance. In the latter instance its formation might have been stimulated by the alcohol, or it might have been due to inanition. The factors producing starvation were furnished by the alcohol.

of gastro-intestinal contents and continued catharsis, re-establishment of all eliminating functions and of normal digestive activity should be undertaken; symptomatic treatment in which hydrotherapy, change of surroundings, diet and occupation should play an important part, is to be instituted. If alcoholism furnished the cause of the epileptic seizures, the usual preventive treatment of alcoholism should be pursued. When changes in the nerve substance have already taken place so that the epileptic phenomena are not any longer the result of acute toxic processes, the usual anti-epileptic measures have to be resorted to*

All other forms of epilepsy with unknown anatomical substrata and not depending upon ingested material, notwithstanding assertions to the contrary, are practically of unknown etiology. There is no particular reason why they should be treated on the principles advocated for the management of intestinal toxicosis and autotoxicosis.

Narcolepsy.

Cases of morbid sleepiness must be probed as to their causation. A variety of disorders, as already pointed out, may occasion pathological sleep. The case of narcolepsy reported elsewhere is unique as to its pathology. The treatment it received afforded no permanent relief.

Objects to be attained: Recognition of underlying

*Withdrawal of chlorin and replacing the same by bromin to avert the epileptic attack, as suggested by Toulouse, Richet and Balint, did not by far prove as successful in my hands as in theirs. It is not at all impossible that the action of bromin is enhanced when little or no chlorin enters the organism; however, it seems to me that the originators of this method have overlooked to study certain facts which must be considered when this mode of treatment is applied.

disorder; its amelioration by specific treatment; increase of bodily resistance and of nerve tonus.

Etiological treatment: Treatment of original disease. If diabetes, by diet; if polysarcia, by diet, exercise, massage and hydrotherapeutic measures; if wrong or excessive nourishment, by regulation of diet; if malaria, by quinin or arsenic; if other acute infectious diseases are at the bottom of the morbid sleepiness, means alleviating the former may be employed.

Symptomatic treatment: Enteroclysis for systemic effects; stimulation of lymph metabolism by hypertonic salt solutions; promotion of general eliminating functions; faradic and static electricity; artificial respiration; massage over cardiac region; strychnin, nitroglycerin, adonidin, caffeine, camphor hypodermically.

Preventive treatment: Continuance of etiological treatment; catharsis; maintenance of normal eliminating functions; mental occupation; change of surroundings.

PSYCHOSES.

The entero-autotoxic attack, we have learned in a preceding chapter, generally gives rise to some psychoses. They are, like the autotoxic attack itself, acute and of limited duration. They generally disperse with the other toxic phenomena and demand no special treatment. In some instances symptomatic treatment besides the general antitoxic management may be called for. Acute psychoses of maniacal character enduring longer than the general autotoxic syndrome respond well to hypodermoclyses of sodium chlorid solution. The infusions have to be administered from five to fifteen

times. From 250 to 1500 Cc of the NaCl solution should be slowly injected at one time.

While some acute psychoses are part and parcel of toxic or autotoxic processes, positive proof of the direct dependence of certain chronic psychoses upon enterotoxins—although an ever-increasing number of psychiatrists incline toward the hypothesis—has till now not been forthcoming. A succession of autotoxic attacks, wrongfully interpreted as chronic autointoxication, may be deemed to furnish the substratum of the chronic psychosis. However, while mild gastro-intestinal disturbances are not infrequent in the psychopath, they rarely call forth toxic manifestations. As a state of chronic enterogenous autotoxicosis is scientifically undemonstrable, and as the chronic psychosis is hardly ever concomitant with the symptom-complex of intestinal self-poisoning, it would be illogical to institute general antitoxic treatment for the amelioration of the chronic psychoses in question.

To the extent only in which autointoxication participates in the promotion of the psychosis, or in which toxic or autotoxic processes supervene during its course is an antitoxic treatment indicated. The chronic disease, perhaps inaugurated by a gastro-intestinal crisis, is not any longer the expression of an autotoxic attack and all endeavors to treat it as such very likely will prove in vain.*

*Of course, the treatment devised for intestinal self-poisoning will afford symptomatic relief in many instances of chronic psychoses. Thus, the appetite, the digestive and eliminating functions may be improved, sleep may be evoked and psychomotor excitability may be diminished. The substratum of the psychosis, however, in all probability remains uninfluenced.

PERIODICAL VOMITING.

Proof is still wanting that periodical vomiting is a disease *sui generis* and that it is the consequence of enterotoxins. Yet, the individual attacks of this rare affection closely resemble the phenomena of simple intestinal toxicosis or of autointoxication. For this reason antitoxic treatment may be adopted when the attacks cannot be cut short by means usually employed in persistent vomiting, viz., absolute rest, ice pellets, morphin, cocain, atropin, bromides, chloral hydrate, etc.† The small intestines should be completely evacuated if possible. Calomel, sodium sulphide or formic acid should be administered as neutralizers. Symptomatically, saline infusions, mild massage to the abdomen, twice or even three times a day, or the employment of hydrotherapeutic measures like the Neptune's girdle, or the alternate application of the hot and cold spray to the epigastric region and that of dry hot air may prove of advantage.

ASTHMA DYSPEPTICUM.

The symptom-complex, asthma dyspepticum, it appears to me, is the result of various conditions mechanically interfering with gastric rotation, with respiration, with cardiac action and the movements of the chest muscles. Autointoxication does not seem to play an important rôle in its production. In its wake, however, we may have CO_2 poisoning and the various phenomena arising therefrom.

---

†If the kidneys should be at fault—a condition which has nothing whatsoever to do with intestinal autointoxication—the various indicated antidotal measures have to be resorted to.

The antitoxic treatment limits itself to the evacuation of the gastro-intestinal canal, the removal of mechanical obstruents, the elimination of air from the lower portion of the oesophagus or from the stomach and the induction of gastric movement and increased intestinal peristalsis.

Symptomatic treatment: Eucalyptus, 0.5-1 Cc (gtt. 8-16) of the fluid extract from three to six times a day; asafetida 0.18 Gm (3 gr.) in pills every two or three hours; amyl nitrite in pearls containing one or two drops; nitroglycerin 0.0006-0.0003 Gm (1/100-1.50 gr.), or in the form of spiritus glonoini (1%) gtt. 1-2.

Preventive treatment: Removal of nasal and other obstructions; regulation of food according to digestive capacity; prevention of mental excitement; continued use of saline cathartics; calisthenics; lung gymnastics; moderate out-door exercise; change of surroundings.

TETANY.

Tetany always proceeds on the basis of some tangible disease of the gastro-intestinal tract. The tetanic phenomena are undoubtedly those of a toxicosis. Whether this is ectogenous, autotoxic or physico-toxic in character, or whether it is a mixed toxicosis to which the various forms of poisoning contribute, cannot be statess with any degree of certainty. Personally, I incline to the opinion that tetany is the result of a simple toxicosis which, at times, may give rise to a more or less serious disturbance of the osmotic equilibrium in the organism. A disturbed osmotic equilibrium is identical with, or will result in what I call a physico-toxic state. At any rate, a simple toxicosis (on the basis of a gastro-intestinal condition favoring abnormal fermentative and dissimilative pro-

cesses) is the precursor of all toxic phenomena which may arise during the prevalence of gastric tetany.*

The treatment of tetany must be in the first instance a treatment of its underlying morbid condition. If helminthiasis appears to be the cause of the tetany-epileptiform seizures the usual remedies employed for its alleviation should be administered immediately after stomach and colon have been evacuated. If the enterium

*The following case of true gastric tetany which I presented before the Manhattan Clinical Society at its February meeting, 1904, will illustrate this contention:

Barbara K., 39 years old, mother of one child, native of Lorraine, first consulted me in October, 1903, giving the following history: She has always been a sufferer from constipation; about three years ago she began to have gastric difficulty. The food would stagnate in the stomach and she would bloat considerably. Belching would relieve the bloatedness to some extent, but not entirely. If she abstained from food for 24 or 36 hours the symptoms would slowly subside. If she would take castor oil she would, while defecating, invariably have a fainting spell lasting from five to ten minutes. For the past year she experienced peculiar attacks. She would have a queer sensation in both hands, after which they contracted. Her knees would also contract and the toes would turn upward. She could not move at the time of the attack, which latter occurred quite frequently, as often as twice and even three times a week, lasting from one to four or five minutes on each occasion. Sometimes she would become unconscious. She would then, as she expressed it, "feint through her fingers." She would be very weak after the seizures and could not attend to her work of housekeeping. She was in the habit of consuming very large amounts of food; she could eat two or three pounds of meat at each meal together with a quart of vegetables and an ordinary loaf of bread. She usually ate two or three loaves of bread during the day; besides this she partook of enormous quantities of cakes, pastry

itself appears to stand in causative relationship to the tetanic manifestations, measures to empty it or to neutralize its contents must be adopted. In case dilatation of the stomach (pyloric or duodenal stenosis) and its various consequences, as stagnation and perverse fermentation of food and the production of large amounts of organic acids are at the foundation of the attacks, special treatment for gastrectasia, viz., evacuation of

---

and fruit. The attacks had never ensued when the stomach was empty, or nearly so. She thinks that there is some food left in the stomach most of the time.

An examination revealed an enormously dilated stomach, a very tymlumantic abdomen, and fecal accumulations. Examination of the gastric contents three hours and a half after ingestion of test meal demonstrated a very high total acidity which was due almost entirely to lactic acid. Besides this, the presence of acetic and succinic acids could be demonstrated. Free hydrochloric acid occurred in very small amounts. Peptic action was very limited, dextrin + +; erythro-dextrin +. Removal of the gastro-intestinal contents, often repeated gastric lavage and the exclusion of all carbohydrates from the diet, caused amelioration of the patient's state of health and cessation of the attacks. Gastric tetany does not supervene as long as she refrains from eating large amounts of carbohydrate matter. The attacks recur, although attenuated to a certain degree, as soon as she freely indulges in starchy and saccharine food.

Another authentic case of gastric tetany I had occasion to present to my class at the College of Physicians and Surgeons, Boston, through the kindness of Dr. Sopher of Wakefield, Mass. The patient, a woman about 45 years of age, had an enormously dilated stomach and very pronounced gastroptosis. Regulation of diet, that is, exclusion of all alimentary substances liable to induce hyper fermentation, and the adjustment of a rational abdominal supporter, have averted any further attacks of tetany.

the gastric organ by means of the stomach tube, a small dietary, etc., should be instituted and kept up for protracted periods.

Symptomatic treatment: For threatened collapse hypodermoclysis of isotonic sodium chloride solution; artificial respiration; strychnin or alcohol hypodermically. For oliguria continued enteroclysis of hypotonic sodium chloride solution. To prevent undue gastric fermentation, phenol, creosote, resorcin, thymol, bismuth salicylate, magnesia usta, etc. For cramps and pain, atropin in increasing doses, if necessary, or lupulin in doses of 0.3 Gm (5 grs.), to be repeated every one or two hours; in long-continued cases, chloroform inhalations.

Preventive treatment: Reduction of total ingesta; complete withdrawal of carbohydrates for the time being; complete withdrawal of fatty substances in a certain proportion of the cases; in stubborn cases introduction of nourishment by enemata exclusively for from four to six days, to be repeated every third week if necessary; hypodermoclysis of hyptonic NaCl solution, 500 Cc twice daily for about one week; in severe cases operative interference (resection, gastro-enterostomy) has to be resorted to.

INFANTILE CONVULSIONS.

A certain percentage of cases of infantile eclampsia seem to be autotoxic in origin. The pronounced form is very much like the epileptic attack and it appears that both affections may be the consequence of a similar intoxication. As soon as the enterotoxic causation of the convulsive disorder is recognized antitoxic treatment should be inaugurated.

Etiological treatment: If the stomach appears to be

the source of irritation it should be immediately emptied by the stomach tube or one of aforementioned emetics. If coprostasis is present the fecal accumulations should be removed by high enemata and enteroclysmic procedures. If the materia peccans is presumably lodged in the small intestines, or if enteritis complicates the clinical picture, neutralizing agents like calomel or sodium sulphide should be given in very small doses until their physiological effects have been secured. A pure preparation of dried yeast, in rather full doses, will occasionally afford relief.

Symptomatic treatment: Chloroform during the attack in very small amounts by inhalation; hot baths to which some spirits of chloroform has been added; injection into the rectum during attack of chloral hydrate, camphor, bromides, garlic, asafetida. During interval, nitroglycerin or atropin hypodermically; sodium chlorid, isotonic solution, by hypodermoclysis.

Preventive treatment: Restriction of amount of food; change of type of nutrients; exclusion of milk fat and replacement of the same by yolks of the hen's egg; open bowels; hot baths to which some spirits of camphor has been added; prevention and treatment of enteric disturbances; continued administration of bromides or camphor, or of both, as in the form of the monobromide of camphor, by mouth or rectum (suppositories).

CHLOROSIS.

Enterogenous autointoxication may be an exciting cause of chlorosis. Chlorosis apparently is one of those conditions in which the morbid effect endures for much longer periods than its underlying, or exciting, cause.

Chlorosis, irrespective of its exciting cause, is the

result of the inefficiency of the hematopoietic organs. Enterotoxins which may provoke the onset of the chlorotic condition are not formed continuously, but paroxysmally. Their further production—although their direct bearing upon the chlorosis itself may be insignificant—should be prevented in order that the action of the therapeutically applied stimulants of hematopoiesis is not interfered with. Here, and only here, antitoxic treatment should set in. It is confined to the relief of obstipation, to daily enteroclyses of sodium chloride solution to which some preparation of eucalyptus may be added, which is to be continued for one, two or more months, and to the stimulation of the emunctories.*

All other treatment (iron and arsenic medication, depletion, etc.) which stimulates the hematapoietic function exerts no direct influence upon the removal of the eventual enterotoxin, nor does it exhibit noteworthy antidotal properties.

PERNICIOUS ANEMIA AND LEUCEMIA.

The theory of the entero-autotoxic origin of pernicious anemia and leucemia, as we have seen, is not well supported. The affections, however, may be ushered in by an intestinal crisis which in turn may furnish the exciting cause of the almost always fatal pathological states.

General antitoxic treatment is practically useless in these affections. At the time when the pathological effects are discernible it is, of course, too late to eliminate, or even to neutralize the materia peccans which, presumably acting as a stimulating agent only, has al-

*The chlorotic conditions arising on the supposed basis of deficient "internal secretions" would demand an entirely different plan of treatment.

ready been removed or disintegrated. In individuals with a "lymphogenous diathesis," prophylactic treatment should be instituted; disorders of the alimentary tract, even the most trifling, should be carefully attended to; coprostasis should not be permitted to occur; the amount of albuminous ingesta should be kept at a minimum and large draughts of water should be habitually taken. A hereditary tendency for pernicious anemia or leucemia may be overcome by the administration of small doses of arsenic, continued for from four to six weeks, twice or three times a year.

CYSTINURIA AND DIAMINURIA.

Cystinuria may appear together with or in the wake of manifold diseases. It may be indicative of retarded metabolic processes. Moreigne[96] denies any casual relation between diamines and the production of cystin and doubts that the latter is of enterogenous formation. Being but manifestations of disease, cystinuria and diaminuria cannot successfully be treated by themselves. The underlying affection must be studied and attempted to be cured. Besides, cystin is entirely innocuous and the poisonousness of the diamin-bodies in the amount in which they are apt to occur in the organism is as yet not demonstrated. However, reduction of diet, continued administration of saline laxatives, enteroclysmata and other procedures keeping intestinal putrefaction and fermentation at a minimum and increasing general metabolism can be but accompanied with beneficial results, both as regards the amelioration of cystinuria and diaminuria, as well as the concomitant pathological manifestations.

INTESTINAL ACETONURIA AND DIACETURIA.

The principal source of intestinal acetonuria and diaceturia seems to be the ingested fatty material, more particularly those fatty substances which contain lower fatty acids, as butter for instance. The acetone bodies are indicative of a poisonous state of the organism—poison in the sense that some organs do not functionate properly—but are innocuous in themselves. The acetone bodies are of true intrabiontic formation as long as they are not introduced in a preformed state.

Inasfar as intestinal acetonuria and diaceturia are only symptoms of a disease, the latter should be treated whenever it is recognized and amenable to therapeutic measures. This, in fact, is the only rational treatment. If the underlying disorder of the alimentary canal cannot be detected, or if it cannot be remedied, resort should be taken to the general antitoxic treatment devised for enterotoxicoses. By such treatment the original affection may even be ameliorated.

The fatty substances should be entirely withheld from the nourishment for the time being. Gradually, some fats, as suets and especially yolks of eggs, may be allowed. Butter and cream should not be permitted for some time after cessation of all undue phenomena. The cathartic salines, in effective doses, should be administered before breakfast, for at least three or four weeks in succession. This should be repeated at certain periods, say every fourth month. The benefit of saline enteroclyses is not a direct one in most instances, as the seat of formation of the entero-acetone bodies is in the small intestines. The alkaline effect of sodium bicarbon-

ate does not appear to diminish the intensity of intestinal acetonuria and diaceturia.

Symptomatic treatment may be indicated for the various manifestations of the underlying disturbance. Among the preventive measures of acetonuria and diaceturia I enumerate: avoidance of surfeit; open bowels; prevention of diarrheal disorders; sufficient amount of sodium chloride in food; small quantity of cream in the milk of bottle-fed infants, particularly during the summer months; limited consumption of butter.

Chapter XI.

TREATMENT OF CATABOLIC AUTINTOXICATION.

1. Simple Retention Autotoxicoses.

Seen from a certain point of view, the great majority of catabolic autointoxications may be classified among the retention autotoxicoses. For the reason, however, that besides retention other factors, of more or less importance, contribute toward the toxic syndrome in most cases of catabolic poisoning, there remain comparatively few instances whose cause may be attributed to uncomplicated retention. Among the simple retention toxicoses, those which are due to insufficient CO_2 elimination by the respiratory tract and to the suppression of the perspiratio insensibilis are the most important.

This is not the place to discuss whether the retained carbon dioxid is the only toxic factor in the ensuing cyanosis, pulse retardation, dyspnea and convulsions—phenomena constituting the clinical picture of suspended respiration. Other catabolic gases may participate in the production of the toxic syndrome. This is especially the case when, at the same time, exhalation by the skin is interfered with.

Whenever CO_2 intoxication is dependent upon an obstruction in some part of the respiratory system, the clearance of the air passages is the first essential, as a matter of course. If this cannot be accomplished, stomach and bowels should be unloaded at once to afford greater freedom to the thoracic organs. As CO_2 retention

due to an obstruction in the respiratory organs concurs with deficient oxygen admission, inhalation of the latter, or of compressed air, according to Senator, may prevent or even cure CO_2 intoxication. Aeration of the blood by continued artificial respiration may slowly overcome the effects of the retained CO_2. This will, as a rule, escape in the ratio in which oxygen is admitted to the blood. The respiratory functions, when in abeyance, will often be induced by throwing cold water on the face, or by inhalation of ammonia or amyl nitrite. To sustain the heart's action massage over the cardiac region, application of heat, especially over the heart, hypodermics of atropin sulphate, 0.0006—0.0012 grm (1-100—1-50 gr), caffeine and sodium salicylate (62.5 per cent caffeine) 0.18—0.36 grm. (3—6 grs), brandy or whiskey, enemata of strong coffee or aromatic spirits of ammonia, should be employed.

It is quite likely that there may be a form of CO_2 intoxication which occurs without the presence of a respiratory obstruent. Here the CO_2 apparently exists in a combination preventing its ready liberation. Carbonic acid intoxication of this kind may be at the bottom of a number of pathological states, but as yet we know of no remedial agents, excepting perhaps the administration of certain salts by intravenous infusion or hypodermoclysis, by which the liberation of CO_2 could be procured.

When the cutaneous structures fail to exhale and discharge effete substances normally eliminated by them, the insufficiency may be overcome by inducing the other

emunctories to vicarious activity.* Anything which in the face of diminished tegumentary function stimulates the general excretory work of the organism tends to prevent or to suppress autotoxic manifestations. In addition thereto, the cause of the skin inactivity must, of course, be removed and any lesion of the integument repaired as speedily as possible. This should be done under aseptic or antiseptic precautions as bacterial invasion sets up an additional toxicosis. There is no doubt that some of the untoward phenomena following burns involving extensive cutaneous surfaces are the consequence of micro-organismic interference. This is especially the case when the toxic symptoms ensue some time after the occurrence of the accident.

2. HISTOLYTIC AUTOTOXICOSES.

AUTOLYSIS.

a. The question of autolysis of protoplasmatic substance is a novel one and has not as yet been considered to its full extent. Autolysis, indeed, may overshadow in importance all other processes of degeneration and may be a much more frequent cause of molecular death than any and all other factors. Its bearing upon the mani-

*It must not be forgotten that tegumentary activity includes also absorption of atmospheric oxygen. Factors affecting the eliminative qualities of the skin also affect its absorptive properties. Thus, insufficient oxygenation may complicate the toxic syndrome. True, O—absorption by the skin is quite limited. Zuelzer (Ein Beitrag zu der Lehre von der Hautatmung, Zeitschr. f. Klin. Med. June, 1904) studying this question, calculates that the total body-surface absorbs per minute from 1.08 to 12.25 cmm. O. Hence, the maximum absorption of atmospheric O by the skin is the one-hundredth part of that inhaled by the lungs.

festations usually considered toxic or autotoxic may not be mediate; its occurrence, however, may result in a train of symptoms, or disease entities, the origin of which it has been the custom to trace to sources of quite a different nature. In other words, various affections, especially some wasting diseases, are thought to be called forth by seemingly well-understood factors when in reality they may be the consequence of autolytic processes of certain tissues and organs. Again, as at the foundation of the various autolyses there is either excessive production or activity of certain substances, or deficiency of "antibodies," they may be enumerated among the autotoxicoses. A number of conditions and diseases of probable autolytic origin hence may be counted among the autointoxications.

The theory of autolysis as a causative factor if disease is as yet too little developed to permit of a rational therapy. It is to be hoped that we will gain a deeper insight into the intrabiontic autolytic processes within the next few years, and that we shall be enabled to devise means to cope with the autolytic degeneration of tissues and organs.

ACIDOSIS.

b. For clinical purposes, acid intoxication may be subdivided into *accidental* and into the *catabolic* types. The former has repeatedly found consideration when dwelling upon intestinal acetonuria and diaceturia and the various diseases whose cause has been ascribed to intestinal autointoxication; the latter is a concomitant of a number of pathological states characterized by loss of body-substance.

Where accidental acidosis ends and where catabolic

acid intoxication begins is clinically not always discernible. Again, it is quite possible that a disease usually accompanied by catabolic acidosis exhibits instead an intestinal acetonuria and diaceturia, or that in grave cases, both types of acid intoxication are found in the same individual.

The discriminating diagnosis, as a rule, may be based upon the following points:

	INTESTINAL ACIDOSIS.	CATABOLIC ACIDOSIS.
Age	Not infrequent in children	Most frequent after middle life
Mode of onset	By gastro-intestinal crisis	Gradual
Duration	More or less transient, ceasing with the underlying disorder	Mostly lasting like its substrate
Significance	Perverse dissimilation of fatty substances in alimentary tract	Alkali deficit in tissues; (anomalous) disintegration of body-fat
Alkali therapy	Not actively influencing the condition	Exerts little or no influence
Materia peccans	The "acetone bodies" (?)	Faulty alkali supply (all acid principles)
Secondary phenomena	Headache, languor, depression, vertigo, vomiting, epileptiform states	Peculiar dyspnea, aphasia, stupor, fatal coma

The acetone substances of catabolic acidosis are either due to synthetic production or they are derived from the body-fat. All *clinical* evidence points to the latter eventuality. Positive proof of a synthetic production has never been furnished, and the experimental data demonstrating the transformation of body-fat into substances of the acetone group are as yet quite scarce.

Autointoxication in the presence of catabolic acidosis is a complicated process. This is understood when we remember that the acetone substances, in the amount in which they exist in the organism at one time, exhibit no toxicity, and that they are practically the result of

nutritive disturbances. For the grave autotoxic phenomena concurring with the acetone bodies and other acid principles, faulty alkali supply to fluids and tissues must be held responsible. It is not so much the acidosis *per se*, which, after all, is not in any way essential for the production of toxic phenomena, but the lack of alkalies, of diffusible salts, that occasions the toxic syndrome. At the bottom of acid intoxication, I maintain, there is either an inability to convey the alkali to the structures in need of it, or else, the salts cannot any longer be sufficiently diffused and ionized in the body liquids.

Diabetic acidosis.—The acid principles generally precede and concur with dyspneic (diabetic) coma. In diabetes the acetone bodies are always indicative of a state of undernutrition. This may be brought about by the one-sided diet which must be pursued in grave cases of diabetes, but it will also ensue, although probably somewhat later, when the nourishment contains abundant albuminous substances and moderate amounts of corbohydrates.

Modus operandi of the production of acetone bodies in the diabetic when fat preponderates in diet: yielding of acetone bodies by the fats, especially by those containing fatty acids of low molecular weight, production of intestinal acetone, thereby loss of fat-aliment. Inability of organism to utilize more than well-defined amount of fat. Underalimentation. Loss of body-substance. Disintegration of body-fat. Production of catabolic acetone bodies."

Modus operandi of the production of acetone bodies in the diabetic when diet contains abundant albumins

and some carbohydrates: yielding of glucose by nutrients. Tissue starvation. Disintegration of body-fat. Production of catabolic acetone bodies."[67]

In whatever manner the substances of the acetone group arise, they do not seem to play an important part in the production of the coma itself. Their presence shows that the organism is wasting away and probably also that the introduced alkalies are not properly utilized. In as far as the preservation of body-substance may go hand in hand with systemic ability of alkali or salt utilization, treatment for the suppression of the acetone bodies, although they may not be direct premonitors of coma, when possible, should be instituted in every case of diabetes.

The *treatment,* in the first instance, should be of a *preventive* character. This is accomplished by keeping the diabetic in a fair state of nutrition. If this proves impossible in the course of time, an inevitable occurrence ensuing sooner or later, the general deterioration should be retarded as much as possible. The waste of the diabetic organism, in fact, may be so gradual that urinary acetone may not appear in excess of 0.25 gram in the twenty-four hours.

If pronounced acetonuria and diaceturia have supervened, attempts should be made, repeatedly, if necessary, to suppress the formation of the acetone bodies, or if this fails, to keep their production at a minimum. By adding carbohydrates to the nourishment the acidosis may decrease for the time being. v. Noorden[68] highly recommends his "oatmeal cure" for this purpose, which is carried out in the following manner: Patient ingests every day for a period of from one to two weeks, to the

exclusion of everything else, a soup composed of oatmeal, 250 gm.; butter, 250 to 300 gm.; some vegetable albumin, 100 gm. A portion of this soup is partaken of every two hours.

There is no doubt that the degree of acidosis is, as a general rule, temporarily reduced when carbohydrates are admitted to the diet. However, they should not be partaken of for more than three or, at the utmost, four days, as otherwise the increased glucose output will make itself felt in a manner not to be misunderstood. A short time after the carbohydrates are discontinued, the acetone bodies are again excreted in similar amounts as before the starchy material was added to the nourishment, and thus, although the carbohydrates may alternately be allowed and discontinued for a few weeks, nothing has been gained in the end. It is true, a fatal issue might have been averted, but whether this was imminent is a matter of mere speculation. On the other hand, the ingestion of carbohydrates, irrespective of the form in which they are taken, whether oatmeal or potatoes, as suggested by Mósse[89], or milk, may occasion vastly more injurious results than if they had not been added to the food.

Furthermore, the oatmeal cure is not only disgusting to the patient, but it does not uphold the claims of its author. Oatmeal, in my experience, is not tolerated any better by the diabetic exhibiting acetonuria than other carbohydrates, such as buckwheat or rice, for instance. Again, the very large amount of butter, 250 to 300 gm. daily, which is to be incorporated into the oatmeal gruel,

contradicts the rationalé of acidosis therapy.* Half a pound of butter, or more, ingested daily, is certainly apt to yield large quantities of acetone in the diabetic; as a matter of fact, I have seen a case after subsisting on the oatmeal-fat-albumin compound for some days in which the intensity of the acetonuria had not only not diminished, but had been appreciably augmented.

If we wish to cope successfully with acidosis without aggravating the diabetic condition we can neither add carbohydrates to the nourishment for any length of time, nor can we in most cases increase the amount of albuminous substances.† Therefore, nothing remains but to turn again to the fats; that is, to such fatty ingesta which contain but small amounts, if any, of fatty acids of low molecular weight.

According to the investigations of Leo Schwarz[70] the fatty acids which may be considered mother substances of acetone bodies are valerianic, butyric and caproic acids; fatty acids of high molecular weight, like palmitic,

---

*v. Noorden himself has shown that unless more than 150 gm. of butter are ingested during the day, the acetone bodies will not increase. If the butter is washed, a process by which it loses its low fatty acids, 180 or even 200 gm. may be allowed without fearing an increased production of acetone substances (Versammlung d. Naturforscher, etc., 1902). In his oatmeal cure he orders the addition of from 250 to 300 gm. butter. Does he really think that the 250 gm. of oat flour suppress the existing acidosis and prevent the yielding of acetone bodies by the over-supply of butter?

†The albuminous ingesta, in grave cases of diabetes, do not only augment the glucose output but are liable to putrefy in the alimentary canal whereby butyric and valerianic acids, the precursors of the acetone bodies, are formed.

stearic and especially oleic acid, yield comparatively little acetone. Butter and cream, hence, are productive of largely increased acidosis, while lard, suet and particularly olive oil do not cause a very marked augmentation of the acetone bodies.

The clinician who is attending a case of grave diabetes, complicated by pronounced acidosis, finds himself in a dilemma. Were he to prescribe a diet consisting of small amounts of proteids and large quantities of lard, suet or olive oil, the patient would soon tire of the regimen, his nutrition would not only be not improved but his digestive organs might become seriously disordered. Besides—and this should not be forgotten—the vegetable oils are, as a rule, not well tolerated if used in excess of the ordinary amounts, and lard (frequently not well borne even in moderate quantities) and beef-suet, cannot be relied upon for suppressing an already existing acidosis, nor to improve the nutrition of the diabetic organism.*

THE "YOLK CURE."

There is only one fatty article of food which I found well adapted to the needs of the diabetic organism during acidosis—the yolk of the hen's egg. I have never seen it produce or increase the acetone substances, or to call forth digestive or assimilative disturbances in advanced

*The suggestion of Schwarz to ascertain in the individual instances, analogous to the tolerance for carbohydrates, that for fatty ingesta, i. e., the amount of the latter which may be partaken of in order that acetone bodies are not produced, is rational enough when severe nutritive changes have as yet not occurred. In advanced cases, however, determination of the tolerance of the commonly used fats would almost be synonymous with their interdiction.

diabetes.* Partaken of in the raw or semi-raw condition fresh yolks may be consumed in almost any quantity without calling forth satiation or fullness.

The rationale of the "yolk cure," which will be described in detail, I attribute, among others to the following four main factors:

1. Palmitin, stearin, and olein, the fat substances of the yolk, occasion but small amounts of acetone bodies; in combination in which these fats exist in the yolk, they yield no butyric acid, or hardly any.

2. The large amount of lecithin, supplied to the organism by the yolk, tends to the restoration of nerve force and the amelioration of the cachectic condition.

3. The occurrence in the yolk of a diastatic ferment assisting in the conversion of amyloid substances introduced by proteids and allowed vegetables.

4. The digestive secretions stimulating functions of the yolk.

The first and second factors are too well understood to be again exploited on this occasion. Concerning the third, Mueller and Masuyama[n] found in the hen's egg, more particularly in the yolk, a diastatic ferment which has the ability of forming erythrodextrin, then achroodextrin, and finally isomaltose. The converting power of the ferment is less pronounced and less acute than that

*The "idiosyncrasy" for eggs not infrequently met with even in healthy persons seems to be evoked in the first instance by the white of the egg. None of the diabetics which I had under my "yolk cure," nor a number of other undernourished patients whose diet consisted largely of yolks, developed an idiosyncrasy for the latter.

of the salivary and pancreatic ferment, but it can diastatize as much as 45% of the food during the day.

As regards the fourth factor, I wish to state that Ssoborow, a pupil of Pawlow, some years ago, demonstrated the marked stimulating influence of the yolk of the hen's egg upon the gastric glands; he found that the amount of gastric juice obtained after feeding yolks to dogs whose stomachs had been isolated, was greater than after ingestion of any other articles of food. Obesersky[72] confirming these observations from the clinical standpoint, concludes that the yolk of the hen's eggs exerts a pronounced influence upon the hydrochloric acid glands of the gastric mucosa and that the yolk not only stimulates the stomach to greatly increased secretory activity, but that its frequent ingestion activitates the acid glands to such a degree that yolks may be employed as digestants in affections characterized by lack of hydrochloric acid. My own observations upon the stimulating influence of yolks on the digestive secretions, which extend over a period of almost two years, substantiating all the contentions of the Russian investigators, will be found elsewhere. (The "yolk cure" in the treatment of the underfed. Med. Rec. Dec 31, 1904.)

The "yolk cure" consists in the ingestion of from 10 to 40 yolks a day, together with a small amount of proteids and the nonavoidable carbohydrates furnished by the latter and certain allowed quantities of green vegetables. As each yolk contains about 5 gm. of fat representing more than 46 calories, it takes about 21 yolks to furnish 1,000 and about 32 yolks to make up 1,500 calories. A diabetic weighing 60 kilos, ingesting 21 yolks a day, would, therefore, obtain in fat alone 16.6 calories

per day and kilos of body-weight; taking 32 yolks a day the average for each kilogram of his absolute weight would be 25 calories. Yolks sufficient to yield from 10 to 15 calories per day and kilogram of body-weight, however, are all that are necessary to be ingested in grave cases of diabetes complicated by acidosis.

The "yolk cure," besides suppressing the acetone bodies, causes systemic and nutritive improvement, and increase of body-weight, vigor, and resistance. It also stimulates body-growth in the diabetic child or adolescent.

The "yolk cure" supplies but very small amounts of nitrogen. However, it is body-albumin saving in a much higher degree than any other dietary regimen. Of course, the excreted nitrogen, while the patient is under the strict "yolk cure" exceeds that which has been ingested; the deficit, however, is so trifling that, practically, it does not need to be taken into account. This is especially the case when the yolk days alternate with "proteid-fat (yolk) days." Again, when the glycosuria is moderate, so that larger quantities of albumin, together with yolks, instead of suet or butter, may be partaken of, a nitrogen deficit may be averted altogether.

The technic of the "yolk cure" is quite simple. The diet on which the patient had been, is at once discontinued; this is best done by omitting the next meal. In the meantime the patient's intestinal tract is evacuated, after which a high saline enema should be administered. When the decline of the patient has been very rapid and when the glycosuria and acetonuria are of a high degree of intensity, the exclusive "yolk cure" must be continued until general improvement has ensued. In other, less

pronounced cases, it may suffice to have a "yolk day" twice or three times a week, while the regular proteid-fat (yolk) regimen is pursued on the other days. In a small percentage of the cases larger amounts of carbohydrates may be permitted when the improvement has continued for some time. The additional carbohydrates should be given in the form of green vegetables, and not in that of flour, beans, rice, or potatoes. In whatever manner the yolk diet is altered, the yolks should continue to displace all other kinds of fat, and a strict "yolk day" should be pursued at least once or twice a week for a protracted period.

A sample of yolk menu is given in the following, showing approximate calories yielded:

	Number yolks.	Calories yielded.	Total calories.
Breakfast:			
Cup of coffee, with two yolks.....	2	92	92
Three boiled yolks.....	3	138	138
Early lunch:			
Egg nog (three yolks, 30 cc. whisky).	3	138	270
Dinner:			
Celery soup (five yolks).....	5	230	230
Spinach, 250 gm., eight yolks.....	8	368	443
Cup of coffee, with two yolks.....	2	92	92
Four o'clock:			
180 cc. sugar-free red wine, one yolk.	1	46	125
Supper:			
One plate soup (soup stock), five yolks	5	230	250
String beans, 90 gm., three yolks....	3	138	150
Total	32	1,472	1,790

In order to avoid monotony, variety in soups, vegetables, flavoring, and seasoning substances should be planned. The following cooking recipes for yolk dishes will be found of service:

PLAIN YOLKS.

Boil, shirr or poach the whole egg—only the yolks should be consumed.

COFFEE.

Stir the yolks of two eggs in a cup, then add one cup of hot coffee, stirring constantly.

WINE SOUP.

Let 150 cc. of red (sugar free) wine and the same amount of water, a little cinnamon and one clove come to a boil. Remove from the fire and stir in the yolks of two or three eggs, stirring constantly. Add saccharin, if desired.

SPINACH AND ALL GREEN VEGETABLES.

Boil in salted water until very tender—drain—add pepper and mash to pulp or press through colander. Then add to each ounce of pulp one raw yolk and mix well.

SALAD DRESSING.

Mix the yolks of six eggs (well beaten) with salt, pepper, one teaspoonful of onion juice and mustard. Add juice of half a lemon.

CELERY AND CAULIFLOWER SOUP.

Boil a stalk of celery (cut fine) in 250 cc. of salted water until very tender—strain and add to the boiling liquid the well-beaten yolks of five eggs. Season to taste.

Cauliflower which has been scalded is put to boil with 250 cc. of salted water, when very tender the whole mixture is passed through a colander and returned to the fire, then the well-beaten yolks of five eggs are added. Season to taste.

SOUP STOCK.

For each plate of soup a quarter pound of shin meat, a quarter pound bone, some celery, parsley, one onion and half of a leek are required. Set on the fire with cold water and boil slowly for five hours. Strain, pressing meat to a pulp so as to extract all the juice. Then add five yolks, well beaten.

EGGNOG.

Mix 30 cc. whisky with 90 cc. water and shake or stir briskly with the yolks of two eggs—add nutmeg, cinnamon or lemon.

All yolk dishes must contain salt in sufficient amount; salt not only aids in the assimilation of the yolk constituents, but is absolutely essential for the proper conduct

of the metabolic and osmotic processes. The patient, as a rule, takes readily to the "yolk cure." I have some patients who, although not eliminating acetone bodies any longer, continue of their own volition two or three "yolk days" in the week, and substitute, as much as possible, yolks for other fatty ingesta on the proteid-fat days.

Generally, obstipation does not supervene while the patient subsists on the "yolk cure." However, if it ensues, high enemas, to be followed by some saline cathartic or a good dose of castor-oil, to be followed by enteroclysis with sodium chlorid solution, should be at once administered.

ADMINISTRATION OF ALKALIES IN ACIDOSIS.

The influence of large amounts of alkalies upon acidosis or, in other words, the alleviation of the alkali deficit by the ingestion of alkalies, as already pointed out, seems to be a merely local and limited one. Of course, the alkali therapy, as long as it does not interfere with digestion, is an innocent procedure and may be pursued as an adjuvant to the anti-acetone diet. However, it must not be depended upon when dealing with a case of catabolic acetone production. In such instances, it is the diet alone by which the desired end may be attained. It is possible that alkali therapy for a time averts the enterogenous production of acetone substances, but it is a mooted question whether alkalies alone, that is when the diet under which acetone has been formed is continued, will bring about cessation of an already active acetone production.

It does not matter what alkali is made use of; it is best to devise a combination exhibiting laxative and eliminating properties. The various alkaline waters, to

which some sodium bicarbonate is added, may also be employed.

When diabetic coma has supervened, alkali therapy as such, is utterly useless. Intravenous injection of sodium chloride or sodium carbonate exerts a transitory influence only. The one drug which in my hands proved of decided value in a number of cases of diabetic coma* is the precipitated calcium carbonate (73). If the patient is still conscious, this agent is administered by the mouth, about two gm. (30 gr.) every two hours. During the calcium carbonate period, a saline cathartic should be given every morning, and enteroclysis of large amounts of sodium chlorid solution should be performed at least once a day. In case deep coma has already set in, the calcium carbonate should be administered by the rectum in doses of from three to four gm. (45 to 60 grs.), every four hours. This should be preceded on each occasion by enteroclysis of sodium chlorid solution. The sodium carbonate is suspended in water by the addition of twenty-five per cent its weight of acacia. From 250 to 1000 Cc of water may be used for each suspension. The injection should have a temperature of about 42°C.

Strychnin camphoricum, 0.0006 gm. (1/100 gr.), or more, may be given hypodermically, every three to six hours, while the calcium carbonate treatment is pursued.

*The rationale of calcium carbonate in diabetic coma is not as yet understood. Calcium carbonate may neutralize the enterogenous acetone substances, or the calcium itself, after liberation of CO_2, may serve as a base with which a toxic substance may unite to form an indifferent compound.

PATHOLOGICAL ACETONURIAS, OTHER THAN DIABETIC.

It has already been stated elsewhere that pathological amounts of acetone bodies appear in a number of conditions in which glycosuria is not present. These morbid conditions, discrepant among themselves, have one feature in common, viz., loss of body-substance. The intensity-degree of nondiabetic acetonurias is usually much lower than that of acetonuria in diabetes, and, as in the latter, a causative relationship between the acetone bodies and the occurrence of toxic phenomena, is by no means established.

The acetone bodies in these conditions, among which I enumerate as the most important carcinomatous cachexia, leucemia, the eclampsia of pregnancy and some febrile affections, are expressive of the same state of affairs as in diabetes, namely of under (perverse) alimentation and bodily decline. That the acetone bodies are not the direct or specific result of the various affections in the course of which they make their appearance, is proven by the facts that they are not invariably associated with the original affection, that grave toxic phenomena like carcinomatous coma may supervene without their occurrence, and that as long as loss of body substance has not ensued, they are never demonstrated in pathological amounts.

The acetonuria of pregnancy is explainable on the ground of augmented fat disintegration, which is the consequence of insufficient nutrition; the maternal organism is frequently not only overtaxed by the demands of the fetus, but its elaborating, assimilative and selective qualities are also often impaired or may even act perversely.

The affections which may be accompanied by pathological acetonurias, should, if possible, be treated by special measures; the acetonuria, not directly evoked by the morbid condition but the immediate result of loss of body material, can only be overcome by supplying the factors which may avert wasting of the organism. The "yolk cure," described in the foregoing, will often produce gratifying results. Alkali therapy may serve a certain purpose, but neither suppresses the acetone bodies nor prevents the occurrence of toxic manifestations.

In all these conditions, the acetone bodies do not represent the exclusive or real materia peccans to which the toxic phenomena are due. They, undoubtedly, frequently concur with the real toxiferous substances; it is even not impossible that therapeutic measures directed against the acetone bodies may, at times, also ameliorate the symptoms of toxicosis.

Chapter XII.

TREATMENT OF CATABOLIC AUTINTOXICATION (CONTIN'D).

C. NUCLEOLYTIC AUTOTOXICOSES.

Speaking of autointoxication by nucleolysis, we must recall: *First,* that the toxic phenomena are not so much due to a toxicity of the nucleolytic products than to the fact of their accumulation in the organism.

Second, that a number of pathological conditions may occur after augmented catabolic nucleolysis without being the result of the nucleolytic products.

Third, that augmented or perverted nucleolysis is synonymous, in most instances, with the accumulation in the body of purins and xanthins.

A rational treatment of nucleolytic autotoxicoses should be directed against the cause of the augmentation of nucleolytic substances and not against the individual manifestations as such. Symptomatic treatment may be instituted as an adjuvant to etiological therapy, especially if it is but a temporary measure; as an independent mode of treatment it should be resorted to in those instances only in which causative treatment—for whatever reason—cannot be applied.

Symptomatic treatment of the various manifestations supposedly due to nucleolysis, administered without paying attention to the underlying affection and for the mere purpose of affording temporary relief, in my

opinion is responsible for more drug habitués than any pathological condition human flesh is heir to.

For all practical purposes, it suffices to know that toxic phenomena may ensue after ingestion of food-nucleins or after disintegration of the nuclei of the living cell. In the latter instance, the augmented or abnormal nucleolytic process itself may already be the result of an autotoxicosis. In neither eventuality will the nucleolytic products give rise to untoward phenomena if they are excreted or dissolved in the ratio in which they are formed. Toxic manifestations (apart from the augmented or perverted catabolic nucleolysis which itself is probably the outcome of toxic occurrences), hence, will supervene only in the presence of impaired renal permeability or in that of reduced solvent qualities of the serum, or in that of an association of both eventualities. The etiological therapy has therefore to take into consideration not only the origin of the purins and xanthins but also the reasons of their accumulation in the organism.

If it is found that purins and xanthins are ectogenous, the foodstuffs in which they are preformed must either be interdicted altogether or limited to comply with the solvent and eliminating qualities of the organism. As the determination of the tolerance for ingested nucleins is a rather difficult task, especially when treatment is started, and as the acute exacerbation demands quick interference, it is best, at the onset, to exclude from the dietary all those substances which may occasion a surplus of nucleolytic products, and to wait with the gradual admittance of foodstuffs containing nuclein bases, until some time after subsidence of the acute manifestations.

If the nucleolytic products seem to be derived from catabolic nucleolysis, nuclein-free nourishment, while not alleviating a perversity of the latter, withholds from the organism an amount of nuclein bases. The solvent and excretory functions of the body may then be able to cope with the endogenous purins and xanthins.

Perverted catabolic nucleolysis, very likely an autolytic process, can as yet be treated only in an empiric manner. Alkalies, contrary to the belief of many clinicians, do not check the anomalous nucleolysis, but increase the eliminating properties. Iodin, and its preparations, and colchicum seem to be among the few drugs which retard or regulate destructive metabolism of body-nucleins.

An agent apparently exerting a specific influence upon catabolic nucleolysis we seem to possess in vaccine virus. Since my first publication[74] on this subject in May, 1901, I had occasion to substantiate my experience by more than thirty additional clinical observations; according to these, successful vaccination almost always promptly disperses "lithemic" conditions not due to the mode of living. Vaccine virus usually relieves the lassitude and the "heavy limbs," so common in autotoxic states. The gait of the patient becomes more sprightly; mental depression and pain vanish; the natural vigor returns and the body weight increases in emaciated individuals.

The solvent qualities of the serum for the product of nucleolysis, it appears, cannot be augmented by artificial means. Numerous medicaments have been recommended for this purpose; if they exert any activity at all in this respect, it must be very limited and of a very transitory character. The particular influence of the best of this

class of agents seems to be the one stimulating and increasing diuresis and to this quality alone their efficacy must be ascribed. For the same reasons that an enduring alkalinization of the body-fluids cannot be accomplished, it is impossible to augment their physiological solvent properties.

For the local deficiency of solvents resulting in the local deposition of uric acid salts—the condition expressing the gouty state—procedures of a mechanical or thermic nature, locally applied, will often bring about the dissolution of the uratic deposit. Such procedures, although breaking up the tophi and alleviating the local inflammatory conditions, do not enhance the solvent qualities of the body-fluids to any extent and cannot be considered solvents in the true acceptance of the term.

The eliminating functions must be stimulated, but care must be taken that the increased burden is not thrown on the kidneys alone. This is a mistake too frequently made by practitioners. A diseased kidney may be able to display increased functional activity for a certain—more or less limited—period, but it cannot bear the unusual strain for any length of time without deteriorating still further. In acute toxic conditions, excessive diuresis may save the patient; in chronic toxemias, especially when the renal organs stand at the foundation of the toxicosis, the permeability of the kidneys, it is true, must be kept at a certain degree, but the burden of increased elimination should be borne by other excretory organs. Of these, the intestines are best suited for the purpose. At any rate, catharsis is an excellent medium by which large amounts of circulating

purins and xanthins may be removed from the organism.*

The saline cathartics, in moderate doses, are well adapted to accomplish this end. The Hunyadi waters, Carlsbad Sprudel salts, Seidlitz powders, Rochelle salt or the salts of lithium, taken before breakfast, may have the desired effect. In suitable cases, calomel or other hepatic stimulants may be administered. Occasionally, somewhat more general effects may be obtained from combinations of various salts. A number of such salt compounds, effervescent, and pleasing to take, are on the market. They usually contain some salt of lithium, and the sulphate, phosphate and chloride of sodium. I am in the habit of substituting sodium pyrophosphate (in proportionate doses) for the sodium phosphate. Increased elimination by way of the intestines should be continued for at least three or four weeks at a stretch;

*Woods-Hutchinson (Lancet, 1902, I.) and others are of the opinion that the lithemic conditions are always ushered in by gastro-intestinal disturbances. This fact speaks again for the necessity of thorough intestinal evacuation. Copious perspiration and profuse diarrhea often act as prophylactics of lithemia by removing the excessive amounts of uric acid and other nucleolytic products. The gouty individual knows by experience that sweating and diarrheal discharges are followed by improvement of the gouty symptoms, and he takes care not to suppress the relief-affording discharge.

Hayem demonstrated that the intestines may exert vicarious function for the diseased kidneys; he found in the villi considerable uratic deposits. The greater the impairment of the renal function the more excretory work must be performed by the enterium. If the degeneration of the kidneys is far advanced, the diarrheal discharges may become so profuse that they assume almost a cholera-like character. (Paczkowski, Autointoxication, 1900.)

it may be repeated every third or fourth month if the lithemic symptoms again make their appearance. It must not be forgotten that the alkalies have neither nucleolysis-preventing nor solvent properties and that their influence upon elimination depends mostly upon their salt action. This, as we know, is but a transitory action. Thus, the salts have to be continued as long as there exists an excess of the nucleolytic products in tissues and fluids of the body.

Enteroclysis of solutions of these salts are, as a general rule, not followed by the same good results than if the salts are taken by the mouth.

Elimination by the skin is enhanced by various thermic and hydrotherapeutic procedures. Sulphur-mud baths seem particularly useful in effecting tegumentary elimination. After subsidence of the acute toxic phenomena, a strict antilithemic diet, so-called, need and should not be adhered to; however, in order to prevent renal irritation, the nourishment should be bland, that is, it should contain the smallest possible amounts of extractive matters, spices and alcohol.

3. Histoenzymic Autotoxicoses.

The treatment of histoenzymic autotoxicoses, that is, of those anomalous states supposedly dependent upon the presence of pathological histoenzymes, or upon a perversion—of any nature—of an "internal secretion," is not as simple and rational a matter as the enthusiasts of organo-therapy are wont to believe. Still, organo-therapy in its widest meaning is not without a certain degree of justification; if it is irrational it is not so much on account of the principles underlying it than on account

of clumsy methods and preparations employed for its execution.

Generally speaking, intoxications in the wake of anomalous internal secretions are due to either an excess or deficiency of glandular activity. The treatment in the former instance should be directed toward decrease, in the latter instance toward increase or compensation of the secretion.

Diminished glandular activity may be accomplished in two ways: (1) by removing the hypersecreting organ —frequently a rather irrational measure; (2) by the administration of agents repressing or inactivating the internal secretion.

The last mentioned procedure, under all circumstances, would be the logical one; however, we have as yet no proof that certain remedies possess such antagonistic properties. Nevertheless, it is not improbable that a number of commonly employed agents evidence their medicinal value by diminishing, or retarding, or regulating, or suppressing certain internal secretions.

The metabolizing function of a gland,* when deficient or entirely absent, on the other hand, may be increased or stimulated by the administration of glandular substance or juice of the analogous organ or of any organ performing vicarious activity, or of any agent—physical

*"*Metabolizing function of a gland*," I think is much more expressive of the specific direct activity of a glandular organ than Brown-Séquard's designation "secretion interne." We have not to deal with secretions in the common acceptation of the term; besides, the *external*, measurable, secretion of a gland may be of secondary importance; its metabolizing function may be its foremost quality.

or chemical—exciting the specific glandular quality. Stimulation of the metabolizing function of vicarious glands by similar means is a therapeutic possibility which may afford relief of toxic phenomena following the suppression of a specific internal secretion.

GRAVES' DISEASE.

(Exophthalmic Goiter; Basedow's Disease.)

Graves' disease presents a symptom-complex which is of an undoubted toxic character. The toxic phenomena are usually ascribed to abnormal or excessive thyroid activity (hyperthyroidism); it is, however, probable that perverted parathyroid function stands at their foundation.

Thyroidectomy, partial thyroidectomy and sympathectomy have been advised as cures of the condition. The operations, especially the radical removal of the gland, although causing subsidence of the toxic phenomena in a certain percentage of the cases, are irrational procedures, being often followed by other untoward symptoms or by immediate death.

The normal function of thyroid or parathyroids seems to be essential for the well-being of the organism. Operative interference should therefore be resorted to only in extreme instances. The more rational way of treating hyperthyroidism would be by an antidotal method. Among the large number of remedies which have been recommended for the treatment of exophthalmic goiter but few seem to exhibit positive antidotal properties. One of the antidotal agents, sodium sulphanilate, is brought forward by Kirnberger[75] on account of its antagonistic effect on iodin. While iodin is only one of the over-produced thyroid elements, its presence in in-

creased amounts may occasion the loss of body-substance inevitable in the course of Graves' disease. Indeed, 10 grams of the drug per day, in divided doses, have given very good results in Kirnberger's hands. His patients gained in weight, their appetite and bodily strength improved, the goiter became smaller in some cases, and the tachycardia was rendered less intense in all instances. The tremor was not influenced by the administration of the agent.

Moebius[76] extolls the value of the serum of thyroidectomized animals in ameliorating Graves' disease, and Burghart and Blumenthal[77] advocate the use of a powder derived from the milk of thyroidectomized goats for the same purpose.

The employment of serum and milk of animals deprived of their thyroid glands seems to be a step in the right direction, as these agents appear to be able to neutralize the circulating poisonous material. They exert, however, no curative influence upon the already existing grave anatomical alterations, occurring in the wake of Graves' disease as a consequence of the chronic intoxication.

The Moebius-serum and Burghart and Blumenthal's milk-powder, which latter is marketed under a copyrighted name, are not indifferent agents in the presence of heart disease. In such cases they should be employed with the utmost caution. In all other instances, untoward results have never followed their administration. As much as 50 grams of the milk-powder has been given per day without any other but the curative effect. The dose of the powder has to be regulated according to the severity of the affection. Some patients improve on

diurnal doses of 5 grams, others need 15 and more grams a day.

Symptomatic treatment may afford relief and is frequently a necessary adjuvant in the management of the toxic syndrome known as Graves' disease. Specific antidotal qualities are, of course, not expected from symptomatic therapy.

MYXEDEMA.

The three varieties of myxedema, (1) pachydermic cachexia, (2) cretinism, and (3) cachexia strumipriva, appear to be the consequence of one and the same fundamental cause, that is, athyroidism, which occurs in atrophy, loss of function or absence of the thyroid gland.

Myxedema is a true autotoxicosis. Of all pathological states ascribed to some disorder of internal secretion, it is the one, the specific cause of which is definitely established. The therapeutic proof again corroborates the etiological assumption.

The antidotal treatment consists in the administration of the absent or deficient element. This is supplied by the thyroid gland or any of its preparations which are of the same value in ameliorating either of the three forms of myxedema.

The thyroid gland of sheep or calves may be given in the raw state, minced and seasoned, added to beef tea or soup, or spread on bread, or it may be lightly cooked or fried. If subjected to the heating process, care must be taken that it is not overdone, for this seems to impair the specific qualities of the gland. From one-half to one gland, twice or three times a week, suffices in most instances.

Instead of the fresh thyroid gland a glycerin extract known as Liquor Thyroidei (P. B.), exhibiting the active principles of the former and containing some phenol, or the powdered desiccated gland, Glandulae Thyroideae Siccae (U. S. P. 1905), possessing the therapeutic virtues of the gland in a similar degree, may be employed. The dose of the glycerin extract is from 0.3 to 1.5 Cc (m 5-23) of the desiccated powder from 0.2 to 0.5 gram (grs. 3-6) three times a day.

It is best to start treatment always with the minimum dose; this may be gradually increased. Not all thyroid preparations on the market are of the same activity and purity. The activity of the gland or its preparations does not depend upon the amount ingested, but upon the contents of the active principles. In some instances of myxedema, thyroid-feeding is not well-borne; such cases, however, are the exception. On the other hand, in conditions other than myxedema, as in corpulency for instance, in the treatment of which thyroid preparations are often employed, the latter frequently cause untoward phenomena.

Among the pernicious results following overdoses, or the accumulation of thyroid, we may have: tachycardia, syncope, vertigo, cephalalgia, tremor and glycosuria. Thyroid medication should be immediately stopped when toxic symptoms have ensued. Gradually and tentatively it may be taken up again, beginning with very small doses as soon as the toxic manifestations have abated. Unless the patient is under a regulated diet so that he is in perfect nitrogen balance, thyroid should not be administered under any circumstances. In order to pre-

vent untoward or hyper-activity of the drug, I am in the habit of adding arsenic and adonidin as modifiers, thus:[78]

℞ Acid arsenous .....0.0005-0.001 gm.=
gr. 1/120-gr. 1-60
Adonidin .....0.0005 gm.=gr. 1-12
Thyroid gland, dry pwd.....0.12 gm.=gr. 2
M. ft. compressed tablet No. 1.

As early as 1895 I observed that arsenic exerts a specific influence upon the activity of thyroid. Patients who took arsenic and thyroid at the same time never exhibited any of the deleterious effects of the latter. My observations have been confirmed by Bédart and Mabille,[79] who did not find palpitation, tremor, etc., following the simultaneous administration of thyroid and Fowler's solution. Adonidin strengthens the heart without exhibiting a cumulative action;[80] its addition renders the thyroid substance a perfectly safe medicinal agent.

PATHOLOGICAL ADIPOSITAS.

The abnormal production of fat in organisms deprived of their sexual glands, or in whom the latter have physiologically or pathologically been altered, is a frequently observed fact.

The tendency to adiposis may be perceived in castrated animals that are neither overfed nor kept in confinement, and the number of women developing polysarcia after oophorectomy or in the climacteric, in spite of moderation in diet and sufficient bodily exercise, is legion.

There is little doubt that the sexual glands, particularly the ovaries, may exert other functions besides those known to us. Ovulation alone does not call forth acceleration of pulse-rate and augmentation of arterial ten-

sion or body temperature, neither does it intensify the systemic processes in general or increase the output of urea—phenomena which are incidental with the precursory stage of each menstrual period.[74] By the removal or in atrophy of the sexual glands their specific metabolizing function (internal secretion) gets lost; concerning the latter's nature and mode of action nothing definite, of course, is known at this day. This much, however, may be said with certainty, that absence of this specific function may occasion various more or less chronic disturbances and anomalic conditions, among which obesity is one of the most important (Stern[81]).

Experimental and therapeutic proof that the normal sexual glands produce a substance preventing the deposition of abnormal amounts of fat, is not lacking. The metabolizing influence of the ovary is demonstrated by ovarian grafting and the administration of ovarian substance in women after oophorectomy. I may here mention one of my numerous clinical observations, taken from my repeatedly quoted article "on the relation of obesity to improcreance."

The uterus and ovaries were removed from a woman twenty-nine years old. She experienced the circulatory disturbances often following this surgical intervention in an unusually pronounced degree. A few months after the operation she began to grow stouter. She became more apathetic from day to day. The circulatory disturbances, although somewhat modified in the course of time, persisted for the next three and a half or four years. One day it occurred to me to give her some tablets of desiccated ovaries which were standing on my

desk. An improvement of her general condition followed speedily. The continued use of tablets of ovarian substance caused some diminution of body-weight. (When starting this medication the body circumference had already declined materially.) The woman has felt at ease ever since.

The action of testicular substance or spermin in these cases is much less marked.

In ovarian substance and oophorin we possess antidotal agents for the treatment of the abnormal state, frequently arising after removal, atrophy or disease of the sexual glands.

ADDISON'S DISEASE.

For fifty years the connection between adrenal degeneration and Addison's disease has been known. The morbid phenomena constituting this systemic affection are now attributed to a deficient or absent metabolizing function (internal secretion) of the adrenals. An efficient or antidotal therapy for this, in almost every instance fatal, malady has not as yet been devised.

By this time I think it is universally conceded that supra-renal extract is of no value in the treatment of Addison's disease. Of three cases of the affection which I had on various preparations of the gland, two succumbed four or five months, and one about fourteen months after treatment was started. It is true, the blood pressure in the three patients increased somewhat under the administration of the preparation; however, the increased tension remained without any noticeable influence upon the general condition. On the other hand, some of the untoward symptoms arising during adrenal-

medication may be ascribed to it. In one of the cases, pronounced vertigo usually set in one and a half hours after administration of one of the supra-renal preparations; if the latter was omitted once or twice, vertigo would not ensue. Boinet[82] observed nervous disturbances and tremulation after too frequent injections of supra-renal material. This untoward action, I think, is due to the increased blood pressure. The normal secretion of the supra-renals is too insignificant to exert any such marked influence upon the blood pressure in the organism, and as it has no cumulative action—it being readily disintegrated in the body—it stands to reason that the introduction of medicinal doses, that is of amounts never circulating at one time in the normal individual, gives origin to the increased blood pressure and the various untoward phenomena. In this respect, adrenal preparations apparently do not differ materially from many other medicinal agents.

The treatment of Addison's disease, in view of the lack of an antidotal substance, is therefore limited to the pursuance of hygienic, dietetic and symptomatic measures.

ACROMEGALY.

The etiology of acromegaly—although the majority of modern observers deem it the result of some disturbance of pituitary activity—is still shrouded in obscurity. The extract of pituitary body which has been employed by a number of clinicians possesses no antidotal properties. Other animal extracts as well as other agents also remain without influence upon the peculiar condition. The

treatment must be entirely of an expectant and symptomatic nature.*

*The intense headache of a case of acromegaly which lately came under my observation and which was associated with very severe diabetes—the patient excreting as much as 1,500 grams of glucose in the 24 hours—was permanently relieved by the administration of atropin 0.0006 (1-100 gr.) three times a day for about two weeks, after all other medicaments had proved of no avail.

Chapter XIII.

TREATMENT OF CATABOLIC AUTINTOXICATION (CONT'D).

4. Combined Retention-Histolytic Autotoxicoses.

CHOLEMIA.

Mild cases of cholemia—if cases of "biliousness" may be called such—should be treated on the same principle as intestinal autointoxication.

Grave instances of cholemia which, happily, are of rather rare occurrence, are probably more intractable to treatment than any other autointoxication. I have never heard of an authentic case of grave cholemia which terminated in recovery. We have no specific treatment for the cholemic autotoxicosis, the fundamental etiology of which—in all likelihood—is a varying one. Active therapeusis, as stimulation of cutaneous and intestinal secretion, venesection, saline infusion, etc.—measures well tolerated and of recognized value in a comparatively large proportion of uremics—cannot be advantageously utilized in the pronounced cholemic, being contraindicated by his enervated and ill-nourished condition.

The direct cause of grave cases of cholemia, among which the malignant jaundice of acute yellow atrophy of the liver is probably the most typical example, must not be looked for in a mere obstruction preventing the outflow of bile, but must be attributed to the cessation of hepatic activity consequential to the disintegration of the cells of the liver. There is no obstruant to remove,

and a therapy designed for the evacuation of the bile passages, the least to say, is useless.

In other cases of cholemia, that is in instances of icterus non-gravis, when an obstruction of some kind stands at the foundation of the toxic condition, attempts should be made to remove or disperse it by hygienic-medicinal means. If such attempts fail to dislodge or subdue the cause of the cholemia, active diaphoresis, diuresis and catharsis should be instituted to check the progress of the toxic state and to maintain the organism in as normal a condition as possible. In suppurative or protracted instances resort must be taken to the surgeon's knife.*

*The following interesting case of Diabetic glycosuria with intercurrent icterus and non-medicamental hæmatoporphyrinuria, which finally succumbed in cholemic coma, was reported by me at the meeting of the American Urological Association in 1904, and published in the American Journal of the Medical Sciences, October, 1904.

Dr. R. L., aged sixty-eight years, a retired clergyman, was seen by me in consultation with Dr. Savage on April 2, 1904. The present physician was first consulted in January of this year on the occasion of a slight accident for which local treatment afforded relief. Some weeks afterward a condition bordering on coma set in. According to the description furnished by the attendant physician and the members of the household, the attack was more in the nature of a stupor; Cheyne-Stokes respiration had not been noticed, and the patient defecated and urinated voluntarily. When out of the stupor, however, he could not remember anything at all about it. The condition was looked upon as diabetic in character, as he had been affected with more or less pronounced symptoms of diabetes for the past three or four years. Examinations of the urine made by patient's physician between January and April occasionally showed the occurrence of small amounts of glucose.

Other abnormal urinary constituents besides albumin, which was never found, were not looked for. Microscopic examination was not deemed necessary.

In the beginning of March the patient developed icterus. The condition was very pronounced and was accompanied by several attacks, or periods, of chills. Temperature elevation had not occurred, but a subnormal temperature was noted on different occasions. The stools during the icteric period were clay-colored, the urine exhibited the features of the icteric state. The medication was symptomatic, no hypnotics of any kind were prescribed. (Sulphonal, trional, and tetronal were never administered.) Examination by me on April 2d revealed a dilated heart, slight pericardial friction, no valvular disease, normal rhythm, very weak impulse. The lungs were apparently normal. Stomach was slightly dilated, no hardness or structural alteration perceivable. The spleen was normal as to size. Colon and other parts of the intestines were slightly inflated, but fecal accumulations were not present. The liver extended about 3 cm. below the costal arch, the gall-bladder was enlarged and freely palpable. The parts adjacent to the liver were hard and caused pain on deep palpation; nodules could not be distinguished. Adhesions of metastatic processes were not detected. Kidneys could not be palpated. The various reflexes, though diminished, were present. The icterus could not be accounted for specifically; a provisional diagnosis of heptatic cirrhosis was entertained.

The patient complained of excessive weakness in spite of tonic medication. He had been on a light diet, including some cereals, which caused occasional intestinal disorders. The icteric condition was very pronounced and uniform. Examination of the urine exhibited the following facts:

Amount for twenty-four hours, 850 c.c.; color very deep red; transparency slightly impaired; odor normal; reaction acid, 0.22°; specific gravity, 1023.5; salts of hydrochloric, sulphuric, and phosphoric acids about normal; salts of oxalic acid somewhat increased; carbancide, 17.85 grams; uric acid, traces; xanthine bodies; traces; creatin somewhat increased; hippuric acid, traces; urobilin, very large amounts; uroxanthin,

traces; serum albumin, traces; biliary acids and fatty matters absent; glucose, glycuronic acid compounds, alcaptonic acids, acetone, and diacetic acid absent. The microscopic examination did not reveal any excessive amounts or normal or any abnormal histologic elements.

The very outspoken dark-red color of the urine and the very large amount of biliary pigment led me to suspect the presence of some other specific coloring substance. Accordingly, the presence of hæmatoporphyrin was looked for. The urobilin, extracted from the urine by a modification of Garrod and Hopkins' process, was treated by the method devised by Saillet, a portion of the acid—ethereal extract was straten with water.

The water takes up the urobilin, but not the hæmatoporphyrin. Another portion of the acid-ethereal pigmentary extract was agitated with 5 per cent hydrochloric acid. The latter takes up both coloring substances. After separation ammonia was added to the dilute acid; this was reacidulated with acetic acid and shaken with sulphuric ether. By this process the hæmatoporphyrin is extracted, while the urobilin remains behind. The hæmatoporphyrin obtained by the two methods was identified by spectroscopical examination. The examination on the days following after April 2d were made by the first method above described, by dissolving out the urobilin with water.

The presence of hæmatoporphyrin was found for fifteen days longer; daily examinations of the urine were made until March 20th. The amount of hæmatoporphyrin, though, gradually decreased until on the sixteenth day its presence could not be demonstrated any longer. The urobilin, however, continued to be excreted in very large amounts. In none of the specimens of urine examined until April 20th could glucose be demonstrated.

On May 14th I made a second examination of the patient. The icteric condition had greatly subsided, but was still of quite a pronounced degree, the patient, whose diet since April 2d had consisted mainly of milk and milk preparations, had experienced less trouble with his intestines, but felt very weak,

and was extremely emaciated, his present weight being 132.5 pounds; two years ago he had weighed 210 pounds. I must mention that the patient's height is over six feet. The urine of this day exhibited no hæmatoporphyrin, but the amount of urobilin was still very large. Glucose was found for the first time on that day, and this to the amount of 7.5 per cent, which, the twenty-four hours' output of urine being 1400 c.c., amounted to 105 grams per day. The patient was put on a very rigid antidiabetic regimen, with the result that on May 21st his urine was entirely free from sugar and he felt himself much stronger. The ferric chloride reaction did not ensue on either occasion. Acetone could also not be demonstrated.

This case is of interest from two points: first, on account of the non-medicamental production of hæmatoporphyrin; and, second, on account of the synchronous, respectively intercurrent supervention of the three symptomatic manifestations; icterus, hæmatoporphyinuria and diabetic glycosuria.

Hæmatoporphyrin occurs in small amounts in normal urine and contributes toward its normal color. Its presence in large amounts is always a more or less abnormal phenomenon. Most cases of abnormal hæmatoporphyrinuria have occurred after the administration of sulphonal, trional, and tetronal. Excessive hæmatoporphyrin output is almost a constant symptom in chronic lead intoxication. Abnormal hæmatoporphyrinuria has been found in a case of Graves' disease, one case of hereditary syphilis, one of gastric ulcer with hæmatemesis, and in a few other diseases. In all these diseases its occurrence was accidental, it having been in no relationship with the original disease. According to Nencki and Sieber (Arch. f. experim. Path. u. Pharm., 1888, 24) hæmatoporphyrin and bilirubin are probably of synchronous production—their seat of formation being the liver cells especially. The readily convertible hæmatoporphyrin is utilized for the synthesis of the hæmoglobin molecule; the non-utilizable bilirubin is excreted with the intestinal contents. These deductions stamp the hæmatoporphyrin as a normal intermediary product of metabolism. Other investigators, however, have concluded that, inasmuch as the normal bile does not exhibit

hæmatoporphyrin, this does not seem to play an important rôle in the organism, and that it must not be considered an intermediary product of the anabolism or an essential product in the physiological disintegration of the coloring matter of the blood.

To determine the place of the abnormal production of hæmatoporphyrin, the individual organs of animals poisoned with sulphonal were examined for the presence of hæmatoporphyrin. This was never found in the spleen, blood, muscles, or marrow, but it could always be demonstrated in considerable amounts in the liver. However, as the liver is an important excretory organ of hæmatoporphyrin, its occurrence therein is by no means proof of its hepatogenous formation.

That hæmatoporphyrin was not the result of any of the remedies, there can be no doubt. Plumbism could also be positively excluded. We may assume, therefore, that if the hæmatoporphyrin was of toxic origin, the toxiferous substance was of intrabiontic origin. Whether the same toxic substance stands at the foundation of the accompanying or alternating symptoms, icterus and glycosuria, is a mooted question. I am inclined to accept the interrelation of the three symptoms in this instance. This is confirmed by the fact that while abnormal hæmatoporphyrinuria was present, the glycosuria which had existed to a greater or lesser degree for some years previously, had ceased entirely, and that after disappearance of the abnormal amounts of hæmatoporphyrin (how soon after could not be determined, as no urinary examination was made between April 20th and May 14th), the glycosuria reappeared, occurring probably in greater intensity than ever before. It appears almost as if one and the same anomaly was the causative factor of the three manifestations, that while icterus set in when chronic glycosuria was present, this disappeared when hæmatoporphyrinuria supervened, and did not recur until the hæmatoporphyrinuria had again vanished. It seems that the disappearance of the glycosuria was dependent upon the presence of the hæmatoporphyrinuria; that is, that the anomalous condition underlying both symptoms could only bring about either of them at one time.

UREMIA.

Contrary to the grave cholemic condition, uremia is quite frequently amenable to treatment. Inasmuch as uremia is the most authentic and most important of all autotoxicoses, I shall dwell on its therapy at somewhat greater length without going into details as to the complete management of the various uremic states. Especially do I wish to pass in review some of the commonly employed therapeutic measures, pointing out when and when not they should be resorted to. I make free use of my article, "Some Points Pertaining to the Therapeutic Management of the Uremic State," which I read at the meeting of the Medical Society of the State of New York in January, 1903.*

The diversity of opinion as regards various procedures and medicinal agents in the treatment of uremia can be ascribed only to insufficient consideration of the original affection on the basis of which it has developed.

Uremia, an arbitrary designation comprising a multitude of phenomena often unlike in character and intensity in various patients and in the same patients at different periods, is not the exclusive result of one and the same causative factor in every instance. True enough, all uremic manifestations depend upon the condition of the blood, but while this exhibits some characteristics which are in a measure common to all types of uremia, the serum of every variety possesses some dis-

* The case stands isolated, as I have not found in medical literature any allusion to the synchronous or respectively the intercurrent occurrence of these three phenomena. Operative interference at this time seemed to be indicated to relieve the tension of fluid in the gall-bladder.

tinctive feature. Responsible for this is not only the different underlying renal condition, but also the specific material of the infectious disease in whose wake uremia may appear, and the decomposition products of the retained substances, the formation, quantity and specific state of which are dependent upon duration of retention, oxidation and the physical condition of the serum.

In the large, white kidney, for instance, the passage of the watery constituent of the blood is seriously interfered with; in contracted kidney there is nothing to prevent its outflow. While at the approach of and during the uremic condition extremes in blood composition may not exist any longer, the sera of uremia on the basis of chronic parenchymatous nephritis are differently constituted in some major points from those of uremia due to interstitial nephritis. The tendency to convulsive phenomena in the one, and to a comatose state in the other variety, may well be explained by the different constitution and physico-electric behavior of the respective sera.

It is not my intention to dwell upon all discrepant features of the various uremic sera; however, in order to demonstrate the necessity of a different and more rational management of the various types of the attack I cannot refrain from briefly alluding to the retention nitrogen, a factor most conspicuous on account of its presence in large amounts in the uremic serum due to interstitial nephritis and by its occurrence in noticeably smaller quantities in the serum of uremia following chronic parenchymatous nephritis or the mixed form of the affection.

Under retention nitrogen in the blood is understood

all the nitrogen remaining in the liquid after complete removal of the albuminous substances. The average amount of retention nitrogen in 100 cc. of normal blood serum, according to Strauss[88], is between 25 and 30 mgs.; in chronic parenchymatous nephritis without uremia the average quantity amounts to 40 mgs. and in the presence of uremia to about 62 mgs. in 100 cc. blood-serum; in chronic interstitial nephritis without uremia a mean amount of 82 mgs. and when uremia prevailed 130 mgs. retention nitrogen were found on the average; in the mixed type of nephritis without uremia in the mean 51 mgs., and with uremia 120 mgs. retention nitrogen in 100 cc. blood-serum were demonstrated. These figures show that in the blood-serum of chronic parenchymatous nephritis about 35 per cent more retention nitrogen is contained than in the normal liquid; that in interstitial nephritis the retention nitrogen in the blood-serum occurs in twice the amount as in parenchymatous nephritis, and that in the intermediate type of the affection there is contained more nitrogen than in parenchymatous and considerably less than in interstitial nephritis. They further evince that the amount of retention nitrogen is increased in the uremic conditions following the three forms of nephritis and that in the uremic serum in parenchymatous nephritis the amount of retention nitrogen occurs in about half the quantity it is found in the serum of uremia arising as the consequence of chronic interstitial nephritis.

The enormous quantities of retention nitrogen in the serum of chronic interstitial nephritis undoubtedly stand in causative relationship to the natural termination of this disease—uremia. In chronic parenchymatous neph-

ritis uremia is not only a much rarer but also a less grave complication. In about 75 per cent of the cases of uremia due to chronic parenchymatous nephritis which have come under my observation I have seen recovery from the first attack. The comparative infrequency and mildness of the uremic seizures due to chronic parenchymatous nephritis are explained by the fact of the relatively small amount of retention nitrogen.

The inconsistency of pursuing the same plan of treatment throughout in cases of uremia so unlike in their manifestations and arising from two (or more) so markedly discrepant substrata is obvious.

CATHARSIS.

In all forms of nephritis excrementitious substances, usually removed by the kidneys, should as completely as possible be eliminated by way of the intestines. Continued mild catharsis often prevents the onset of uremia.

The saline laxatives in small doses, by keeping up a mild catharsis and diuresis, are of great importance in the treatment of the pre-uremic stages of nephritis. They withdraw the retentia from the blood, but also large quantities of water. Care must be exercised that the administration of the cathartic salts does not render the stools too watery, as this is a positive proof of the withdrawal of much water from the blood and hence also of the latter's continued or even augmented hyperosmotic state. The hydragogues should not be given for any length of time, especially not in the uremic state occurring on the basis of chronic interstitial nephritis. Enteroclysis with weak saline solutions is to be preferred to the administration of salines by the mouth when uremia threatens.

As soon as the premonitory signs of uremia make themselves evident active purgation should be instituted. This, however, should not be continued after the bowels have become thoroughly emptied. A full dose of castor oil, taking everything into consideration, is probably safer to administer and better adapted to effect rapid evacuation of the intestines in threatened uremia of whatever origin, than any other single agent. Pending the action of the castor oil a high rectal enema of soap suds and olive oil may be applied.

DIAPHORESIS.

Promotion of the activity of the sudoriferous glands to enhance the excretion of retentia is indicated under certain restriction in every instance of acute uremia. It has proved of special value when employed soon after the onset of the uremic phenomena. When the attack has persisted for some time, or when a pronounced comatose condition has supervened, sweating, as a rule, is of little or no avail. For reasons already stated, its application has a greater salutary and more lasting effect in uremia having chronic parenchymatous nephritis at its foundation; it is essential that it should bring about the desired result in a short time; too long continued, particularly after marked symptoms of improvement have made their appearance, its beneficial influence at first noticeable, may cease, or it may become a directly harmful agent. That is, by free perspiration considerable amounts of excrementitious substances may be removed from the serum and the watery accumulations; the quantity of water, however, by the medium of which the solids are excreted, is in proportion larger than it exists

in the blood. This is evinced by the molecular concentration of the blood-serum, which is most always higher than that of sweat. Withdrawal of indefinite (because unmeasurable) large amounts of water from the serum, in other words, tends to increase still further its hyperosmotic condition and to decrease its conductivity.

If sweating is kept up by active measures, enteroclysis with a weak sodium chlorid solution, or hypodermoclysis with a hypotonic solution of NaCl should be performed at certain intervals.

The best method of inducing diaphoresis is by the application of uniform heat. Steam, or dry heat or the hot wet-pack may be used for that purpose. The patient should be exposed to the heat for from fifteen minutes to one hour at the time, according to his condition. Before the heat is applied I generally let the patient take a large draught of freshly-made hot but weak infusion of Linderae Cortex (spice-bush bark), which is an excellent, and at the same time innocent sudorific. Hot lemonade will also be found serviceable. On the other hand, diaphoretics like pilocarpin, whose employment is always connected with a certain amount of risk—especially in uremia—should only be resorted to when other means have failed.

VENESECTION.

Abstraction of blood is a therapeutic measure of transitory value mostly, but serving a good purpose in many instances of uremia. The most lasting results of bleeding are obtained in cases following acute nephritic conditions; that is, in such instances in which the patient is still sthenic and in which the blood has not as yet attained that degree of admixture and impoverishment

which it exhibits during the chronic renal affections. Furthermore, uremic manifestations on the basis of chronic parenchymatous nephritis yield more readily to venesection than those which are due to contracted kidney. In children, abstration of 100 cc. to 250 cc. of blood often effects immediate improvement; in adults not less than from 150 cc. to 250 cc. and if the condition of the patient warrants it, 300, 400 or even 500 cc. of blood should be withdrawn at the time.* When the uremic symptoms do not abide after venesection, the procedure may be repeated on one and the same day, provided the patient (apart from the uremic state) is yet in a comparatively fair condition and the uremic manifestations are the result of an acute renal disturbance. In asthenic and far advanced cases, on the other hand, abstraction of blood is not only useless as a rule but often even injurious.

The frequent salutary results of venesection in the properly selected cases cannot be ascribed to the abstraction of a few hundred cubic centimeters of blood and the proportionate quantity of retained nitrogenous material; furthermore, withdrawal of blood does not in the least interfere with the molecular concentration of the remaining blood nor does it tend to increase the electric conductivity of the blood-serum. We possess no definite information that after blood-letting oxidation is enhanced, a process by which the retentia could be transformed into innocuous substances. Such a transforma-

*It seems that we have become rather timid as regards phlebotomy in uremia. In the full-blooded oftentimes 750-1000 cc. (and more) of blood must be abstracted to obtain satisfactory results.

tion—if it really occurred—could probably reduce the "virulence" of uremic blood in a chemicotoxic sense but it would not materially alter its physicotoxicity. The improvement afforded by venesection is likely due to nothing else but the relief of the vasoconstriction in the kidneys or in the central nervous system or in both these places.

Instead of venesection, *venepuncture* may be performed. For this purpose the venepuncture needle of Strauss, or that of the author, may be used. Strauss's needle is nothing else but an aspirating needle in the canula of which a small handle is attached vertically. The needle of the author (Stern's trocar) is constructed on the principle of the trocar, which, when in situ, with withdrawn perforator, cannot injure the bloodvessel as Strauss's needle is apt to do. The advantages of venepuncture over venesection are: greater simplicity; greater safety; greater convenience, both for patient and physician; greater cleanliness; more rapid accomplishment of the purpose; possibility of immediate intravenous saline infusion after abstraction; rapid healing of the small puncture wound. Strauss was able to puncture and needle the vein in almost 95 per cent of all cases in which depletion was to be performed. My experience tallies about with his. In such cases only when the arms are very fat or when on account of an edema the course of the vein cannot be recognized, it becomes necessary to perform venesection.

The chance of injuring nerves and arteries is reduced to a minimum by inserting Stern's trocar into the cephalic vein, which is not situated in as close a prox-

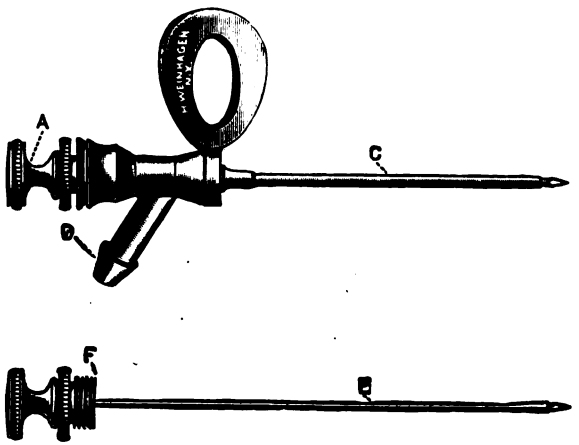


FIG. I. VENEPUNCTURE (STERN'S) TROCAR.

A—Trocar. B—Thumbrest. C—Canula. D—Solution Inlet, Blood Outlet. E—Perforator. F—Packing Box Cap.

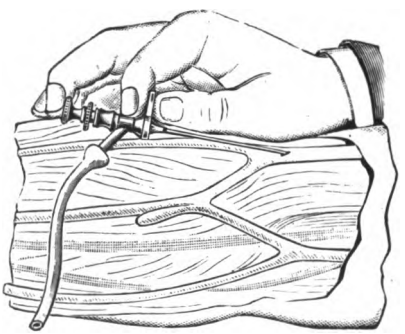


FIG. II. METHOD OF INTRODUCTION OF STERN'S TROCAR INTO THE CEPHALIC VEIN.

FIG. III. GLASS-CONNECTING TUBE.

imity to these as the vein generally chosen for venesection—the median basilic. The vein in either arm may be punctured; however, if the vein on the left arm is not more prominent, it will be found more convenient to needle the cephalic vein of the right arm. The puncture is made so that the point of the trocar is toward the axilla; although the circulation occurs in the opposite direction the blood flows out readily. The arm is corded as in venesection, a piece of rubber tubing serving the purpose. The rubber tubing should be drawn sufficiently tight to make the veins stand out prominent, but not so tight as to suppress the radial pulse. Immediately after depletion when the cording has been removed and the canula is still in situ, the saline infusion may be administered through the latter.

HYPODERMOCLYSIS AND INFUSION.

Subcutaneous or intravenous introduction of a weak solution of sodium chlorid dilutes the blood, produces diuresis and compensates for the amount lost by the artificial abstraction. The effects are more or less transitory in character, but may endure sufficiently long to bridge over a critical phase in the uremic attack. Intravenous injection, of course, acts more rapidly and vigorously than when the solution is introduced by hypodermoclysis, but its effects are correspondingly less lasting. A sodium chlorid solution which is isotonic to human blood contains 0.91% NaCl. It is the true physiologic salt solution and its intravenous injection after severe hemorrhage is followed by regeneration of the blood-plasma and restoration of the normal volume of blood. In uremia, however, it has been observed that an isotonic sodium chlorid solution does not act as efficiently

as one which is hypotonic. For this reason a decinormal NaCl solution containing not quite 0.6% of the salt is usually employed in this condition. This is understood when we remember that the high osmotic tension of uremic serum is not so much due to its ionized as to its neutral molecules.

To effect a more general ionization and conductivity water only is essential. We do not need additional electrolytes in the uremic serum which are introduced from without, but we should inject a solvent to facilitate dissociation of the electrolyte molecules existing in the blood. As plain water, however, may call forth too pronounced hypotonicity, and as it is a poison to the erythrocytes, producing their crenation, a weak solution of NaCl should be resorted to. I have used a 0.5%, and now for some time a 0.35% solution with the utmost benefit to the patient, especially in uremia due to chronic parenchymatous or acute nephritis.

The comparatively small amount of nitrogenous retentia in the uremic serum in diffuse nephritis facilitates the reëstablishment of its normal conductivity after subcutaneous or intravenous injection of the salt solution; on the other hand, in uremia having chronic interstitial nephritis as its foundation, when the retention nitrogen exists in enormous quantities, and when ion formation and ion movement are more or less paralyzed, not alone water but also goodly amounts of active molecules seem to be indicated. This, however, I wish to have understood as a hypothetic suggestion only, for it is an extraordinary fact that I cannot assign the improvement in any single case of uremia due to interstitial nephritis to the influence of the sodium chlorid solution

alone, whether I administered it in hypotonic or isotonic solution, by hypodermoclysis or intravenously.

The minimum amounts of the solution to be used should never be less that 125 Cc., if injected intravenously, and 250 Cc., when administered by hypodermoclysis. Smaller quantities, if at all, produce very limited and rapidly passing effects only. The maximum quantity of decinormal sodium chlorid solution which may be administered in the uremic state must in some way correspond to the amount of blood withdrawn. At one time it should not exceed 750 Cc., if employed subcutaneously, and not more than about one-third of this if introduced by infusion. The procedure, however, may be repeated as often as phlebotomy is performed. When a considerable amount of blood has been abstracted it may at times be necessary to repeat the introduction of the saline solution at short intervals.

As serum conductivity is enhanced by elevation of its temperature, additional benefit will be derived if the saline solution when entering the organism exhibits a temperature above normal blood heat. If utilized by hypodermoclysis it should possess a temperature of from 40° to 41° C. (104°-106° F.) at the moment it enters; injected by infusion it may safely be introduced into the vein at a temperature of from 45°-48° C. (113°-118° F.)

ADMINISTRATION OF MORPHIN.

When after the employment of chloroform, vasoconstriction and convulsive phenomena do not diminish, small doses of morphin, although not exhibiting any antidotal properties, may be resorted to. In uremia of acute nephritic states, more particularly, it may tend to bridge over a critical period. Its eventual efficacy

in controlling uremic convulsions may be due to its retarding the metabolic processes, thereby preventing further accumulation in the blood of catabolic substances, and to its augmentation of vascular tonicity. Convulsive manifestations arising on the basis of chronic parenchymatous nephritis also frequently decline in intensity or cease altogether after the injection of morphin.

Uremia of chronic interstitial nephritis, characterized in almost every instance by a condition of tranquil coma, very rarely exhibits convulsive phenomena. In the absence of such manifestations there is no occasion at all to employ morphin, and the existence of a comatose state a priori precludes its administration.

While, therefore, morphin in small doses is innocuous in uremia of acute renal disease and chronic parenchymatous nephritis, and may be a factor in effecting subsidence of convulsive symptoms, it is not indicated in uremia of chronic interstitial nephritis which presents an entirely different clinical picture, but being comagenous itself, may aggravate the existing comatose condition and hasten a fatal issue.

OTHER MEDICINAL AGENTS.

Inhalations of chloroform are sometimes called for to mitigate the convulsive attacks. The drug gives prompt relief in many instances. In as far as chronic interstitial nephritis is usually not accompanied by convulsions, chloroform is as a rule not employed in the uremic state arising in its wake. In cases where it is indicated, chloroform may be given with impunity. The same may be said of ether which is either given by the mouth (4 Gm.=3i, every 30 to 60 minutes), or by deep

injection into the tissues (2 Gm.=3ss every hour or two), which latter is painful; this, however, is of no consequence when coma has supervened. Generally speaking, in the instances in which morphin may be an efficient agent, all other comatogenous and anticonvulsive drugs, as chloroform, ether, chloral hydrate, potassium bromid, etc., may also prove of special value.

PUERPERAL ECLAMPSIA.

The eclamptic attack, a genuine autotoxicosis, cannot always be assigned to the selfsame cause. A rational treatment of the convulsive seizure is possible only if some opinion is formed concerning its individual pathological substratum. The discrepant ideas entertained by obstetricians as regards the value of certain therapeutic procedures for the relief of the eclamptic condition is due—in a measure at least—to the non-classification of the various instances. There are at least three types of puerperal eclampsia.

1. *Cases consequential to chronic nephritis.*

   In these the eclampsia is of a uremic nature; the prognosis is bad. Treatment depends on the microscopic findings, which are very likely those of chronic parenchymatous nephritis. Interstitial nephritis occurs as a rule without convulsions and in older women. Mixed type of nephritis not uncommon.

2. *Cases consequential to passive renal congestion or to an acute nephritic condition.*

   These, according to Roberts,[84] are usually cases of primiparae; the manifestations are likely in part uremic and in part reflex; the prognosis is

not so unfavorable as in the former type; active depletive treatment should be instituted.

3. *Cases consequential to extra-renal causes (Stern).*

In these instances the urine may or may not contain albumin; if pulse is strong, full and bounding depletion is called for; if this it not the case, morphin, chloroform or ether anesthesia, veratrum viridi, or full doses of chloral hydrate or potassium bromid may be serviceable.

The appearance of albuminuria does not invariably point to the renal organs as the chief and only cause of the eclampsia. In all instances in which, besides the albumin, no evidence of chronic or recent kidney disease can be discovered by the microscope, it is well to think of some extra-renal cause of the convulsive seizures. I have always maintained that faulty activity, or a disease, of the liver stands at the foundation of many a case of eclampsia. Whenever the presence of renal disease cannot be definitely determined, it is advisable to apply, in addition to the anticonvulsive agents, a general treatment for intestinal autointoxication.

The proper obstetrical treatment, of course, is of preeminent importance.

APPENDIX.

GLOSSARY.
REFERENCES.
INDEX.

GLOSSARY

In the following explanatory vocabulary, which is added in the interest of greater practicability of this little book, the author wishes to convey his understanding of some words and phrases that have found employment in the text:

ACID INTOXICATION—Poisoning by overproduction or deficient neutralization or abnormal retention of, or by pathological, acid principles.

ACIDOSIS—Same as *acid intoxication*.

ADDITION—The (hypothetic) fifth protective reaction in the organism; the combination of a toxic substance with a metabolic product ensuing without dehydration.

ADIPOLYSIS—The chemical decomposition of body-fat.

ADIPOLYTIC—Pertaining or caused by *adipolysis*.

ADIPOSITAS—Obesity, fatness, polysarcia, corpulency.

AEROPHAGIA—The swallowing or sucking of air, common in hysteric subjects, often causing distress in the stomach and intestines.

ALIMENTARY TOXICOSIS—Poisoning by substances elaborated from ectogenous material.

AMBOCEPTOR—An immune agent with two haptophorous groups, one group combining with the substrate, the other with the proteolytic ferment, "the complement."

AMYLOLYSIS—Conversion of starch into dextrin and grape sugar.

AMYLOLYTIC—Relating to or causing *amylolysis*.

ANTIBODIES—Substances, circulating in the blood, rendering innocuous toxic material which has found its way into the circulation.

ANTIKINASE—An *antibody* inhibiting the formation or activity of a ferment or enzyme.

AUTOCHTHONUS INTOXICATION—Intoxication native to the soil, *i. e.*, endogenous intoxication. See *endogenous*.

AUTINTOXICATION, CATABOLIC—A morbid condition, the direct or remote result of retained and accumulated, of incompletely or perversely converted, or unattenuated, or non-dissociated, or irregularly-combined substances, derived from beyond the stage of anabolism.

AUTINTOXICATION, INTESTINAL—A pathological state, more or less transitory, supposedly due to the absorption of intrabiontic poisons from the alimentary tract.

AUTOINFECTION—An infection due to bacteria, or their toxins, derived from the individual's own body. Reinfection.

AUTOINTOXICATION—*Autintoxication, autotoxicosis*—self-poisoning by the pathological absorption or retention of intrabiontic products. ducts.

AUTOLYSIS—Self-destruction of organic tissues; auto-digestion; localized intra—and intercellular catabolic changes independent of general metabolism.

AUTOPROTECTION—The self-defense of the organism against noxious influences.

CARBAMID—Carboxyl amid. Urea.

CARBONIC ANHYDRIDE—Carbon dioxide; acid carbonic.

CATABOLISM—The opposite of anabolism; retrograde tissue metamorphosis; normal destructive disintegration; every intracellular process beyond the stage of anabolism.

CATALYSIS—A chemical alteration ensuing in a compound by the action of an agent which itself does not undergo any change.

CAUSA MORBI—The cause of disease.

CHEMICO-AUTOTOXICITY—The quality of being autotoxic through chemical agents.

COMPLEMENT—An additional substance, nonspecific *per se*, but rendering active the immune bodies in fresh serum. (Addiment.) It exhibits all the characteristics of a ferment.

CRYPTOGENIC—Concealed.

CRYPTOGENIC ACID INTOXICATION—An indefinite term mostly employed to denote acid-poisoning of gastro-intestinal origin.

DEUTEROPATHIC—Pertaining to an affection that is secondary to another.

DIHYDROGEN SULPHATE—Sulphuric acid.

DYSCRASIA—An anomalous state of general metabolism reflected by an abnormal or pathologic condition of the blood.

ECTOGENOUS—Developed outside the host.

ELECTROLYTE—A substance dissociating when dissolved in water, *i. e.*, salts, strong bases and acids. The result of electrolytic decomposition are the ions which conduct the electric current in a liquid.

ENDOGENOUS—Originating, being produced, within. *Endogenous causation of disease, i. e.*, diseases the causative factors of which have arisen in the organism. Not necessarily an autotoxic disease.

ENTEROCLYSIS—Intestinal irrigation.

ENTERON—Intestinal tract, especially the small intestines.

ENTEROKINASE—An amboceptor or complementary substance which, when added to trypsinogen, causes the production of trypsin ferment.

ENTEROPRODUCT—Any substance elaborated in the alimentary canal.

ENTEROTOXIN—Loosely applied to any noxious substance originating in the intestines with or without participation of body-cell activity.

HISTOENZYME—A substance contained in any "internal secretion" exhibiting enzymic qualities. It may be of physiologic or pathologic occurrence.

HYDROLYSIS—The decomposition of a substance (and the formation of new compounds) by the absorption of water.

HYDROLYTIC—Pertaining to *hydrolysis.*

HYDROTHIONEMIA—A term denoting poisoning with sulphuretted hydrogen. *Hydrothionuria.* H2S may be produced (1) in the urinary organs by the activity of bacteria upon the so-called neutral sulphur of the urine, or (2) in the intestines from the sulphur-containing aliments, or (3) in any place of the body by certain microorganisms (Proteus, pyogenic bacteria).

HYPERGLYCEMIA—Abnormal amount of grapesugar in the blood.

HYPEROSMOTIC—Hyper-isotonic, pertaining to solutions of higher osmotic pressure than that of the plasma.

HYPOSMOTIC—Hypo-isotonic; hypotonic; pertaining to a solution whose osmotic tension is lower than that of the plasma.

IDIOSYNCRASY—A characteristic peculiarity depending upon constitutional causes.

INFECTION—The direct or indirect transmission of disease-germs to an organism.

INTERNAL SECRETION—The secretion of a glandular organ, containing specific elements, and which is supposed to be transmitted to the blood or lymph; metabolizing function of a gland.

INTRABIONTIC—Within the organism (in the sense of being part and parcel of the organism).

INTRABIONTIC POISON—A term denoting a noxious substance produced within the organism with the participation of the body cells.

IODISM—A condition called forth by the prolonged therapeutic exhibition of iodin or its compounds (frequently insufficient elimination), and characterized by symptoms alike to those of acute coryza, redness of the conjunctiva and the mucosa of the respiratory tract.

ISOTONY—The equimolecularity of two solutions. The condition of being isosmotic, *i. e.,* solutions exhibiting an identical degree of osmotic tension.

KINASE—A substance rendering active a ferment or enzyme.

LYMPHAGOGUE—An agent augmenting the production or excretion of lymph.

MATERIA PECCANS—Disease-producing matter.

METABOLISM—The constructive (anabolic, assimilative) and the destructive (catabolic, dissimilative) processes upon which the nutrition and function of living matter depend. The intrabiontic osmotic and oxidation processes are part and parcel of general metabolism.

METABOLIZING FUNCTION (OF A GLAND)—See *"Internal Secretion."*

MOLECULAR CONCENTRATION—An expression indicating the number of moles (gram-molecules) contained in a liter of fluid irrespective of an eventual dissociation.

NUCLEOLYSIS—Disintegration or destruction of any nuclein substance (body nucleins, nutriment nuclein).

NUCLEOLYTIC—Pertaining or caused by *nucleolysis*.

OSMOLOGY—The science concerning the physical conditions of and in the body fluids.

OSMOSIS—Osmose; the exchange, or tendency to exchange, of the soluble material of two liquids separated by a semi-permeable membrane.

PHYSICO-ELECTRICAL EQUILIBRIUM—Osmotic equilibrium; the inter-relation of the physical conditions of the various body-fluids which is essential for the normal performance of the vital processes. This inter-relation does not consist in the equality, but in the physiologic dissimilarity, of the osmotic conditions in the different fluids.

PLASMOLYSIS—The disintegration or destruction of protoplasmic material (body-protoplasm).

PLASMOLYTIC—Pertaining or causing *plasmolysis*.

POLYSARCIA—Excessive fleshiness, fatness, obesity.

PROTOPLAST—The primitive, undifferentiated, protoplasmic unit.

RETENTION NITROGEN—All the nitrogen remaining in the blood after complete removal of the albuminous substances.

SECERNATION—Secernment; secretion (glandular).

SEROTOXICITY—Poisonous state of the serum.

SIALOGOGUE—Ptyalogogue; an agent increasing the production or excretion of saliva.

TARTRONYL CYNAMID—Uric acid.

TOXALBUMIN—Any poisonous proteid substance; in a more limited sense the toxic products, resembling ferments, which are due to the activity of bacteria upon the body albumin.

TOXIFEROUS—Conveying toxic material.

VENEPUNCTURE—The direct puncture of a vein by a specially constructed needle or trocar for therapeutic purposes.

ZYMASE—The enzyme in the yeast effecting alcoholic fermentation.

ZYMOGEN—The forerunner of an active ferment or enzyme. The undeveloped, latent, ferment deposited in the cells.

REFERENCES*

1. Bouchard: Leçons sur les auto-intoxications dans les maladies. Paris, 1887.

2. Petters: Acetonurie, Prager Vierteljahrsschrift Band LV., 1857.

3. v. Voit: Zeitschrift für Biologie. Band VI, VII, etc.

4. Schmiedeberg: Centralblatt für die Medicinische Wissenschaft. 1868, S. 497, und Archiv für Exper. Pathologie und Pharm., Band XIV.

5. Naunyn: Archiv für Exper. Pathologie und Pharm., Band XXI, and elsewhere.

6. v. Jacksch: Ueber den gegenwärtigen Standpunkt der Lehre von der Vergiftung. Wiener Klinische Wochenschrift, 1890, No. 52.

7. Senator: Die Autointoxicationen und ihre Behandlung. Die Deutsche Klinik am Eingange des 20. Jahrhunderts. Band I, S. 19, 1901.

8. Drucbert, J. et Dehon, M.—Echo med. du Nord. 6. 137-139.—Jahresbericht ueber die Fortschritte der Tier-Chemie ueber das Jahr 1902.

9. Oppenheimer, Carl,—Die Fermente, etc. 2te Auflage. Leipzig, 1903.

10. Weinland, E.—Ueber Antifermente, etc., Zeitschr. f. Biologie 44, 1-15 and 45-60.

11. Fromm: Die chemischen Schutzmittel des Tierkörpers bei Vergiftungen, 1903.

12. Lewin, L. Lehrbuch dev Toxikologie. 2te Auflage, 1897.

13. Ewald,—Die Autointoxication.—Berl, klin. Wochenschr. 1900, Vol. XXXVII, p. 133 and 166.

14. Senator,—Ueber Hydrothionaemie und ueber Selbstinfection durch abnorme Verdauungsvorgaenge.—Berl. klin. Wochenschr. 1868, No. 24.

15. Tommasoli: Schema einer neuen Klassifikation der Hautkrankheiten. Ueber autotoxische Keratodermiten, Dermatolog. Studien, 15, Heft, 1893.

*For other references see the footnotes throughout the book.

16. Furet: De la Narcolepsie. These de la Faculté de Paris, No. 303. Roussel.

17. Sainton: Gazette hebdomadaire de Médicine et de Chirurgie. 1901, 34.

18. Stern: A Contribution to the Pathogenesis of Narcolepsy and Other Forms of Morbid Sleepiness. Med. Rec., Jan. 11, 1902.

19. Leyden: Ueber periodisches Erbrechen, etc. Zeitschr. f. klin. Med., 1882.

20. LeRoy: Therapeutic Gazette, June, 1902.

21. Edsall: A Preliminary Communication Concerning the Nature and Treatment of Recurrent Vomiting in Children. Amer. Jour. Med., Sciences, April, 1903.

22. Albu: Ueber die Autointoxicationen des Intestinaltractus. 1895.

23. Stern: The Clinical Importance of Aerophagia. N. Y. Med. Jour., Feb. 20, 1904.

24. Monti: Kinderheilkunde in Einzeldarstellungen. 3. Band, 1903.

25. Kussmaul: Zur Lehrvon der Tetanie. Berl. klin. Woch, 1872.

26. Duclos: De l'origine intestinale de la chlorose. Rev. Gén. de Clin. et Thér., 1877.

27. Conturier: Des rapports de la chlorose avec la dilatation de l'estomac. Thèse de Paris, 1888.

28. Charrin: La chlorose. Gazette hebdomadaire, 1. 1896.

29. Clark: Observations on the Anaemia or Chlorosis of Girls. Lancet, 1887.

30. Nothnagel: Ueber Chlorose. Wiener med. Presse, No. 51, 1891.

31. V. Noorden: Die Bleichsucht. Nothnagel's specielle Pathologie und Therapie. VIII. Band, 2. Theil.

32. Forchheimer: The Intestinal Origin of Chlorosis. Am. Jour. Med. Sci., 1893.

33. Vehsemeyer: Internationale klin. Rundschau, Nov. 25, 1894.

34. Koettnitz: Peptonurie bei einem Falle linearer Leucaemie. Berl. Klin. Woch., 1890.

35. Moerner: Zeitschr. f. Physiolog. Chemie. 1899.

36. Baumann und v. Udransky: Ueber das Vorkommen von Diaminen bei Cystinurie. Zeitchr. f. physiol. Chemie. Bd. XIII 1889.

37. v. Noorden and Mohr: The Acid Autointoxications. Translated by Croftan, 1903.

38. von Dieterichs, Wiener medizin, Wochenschr. Nov. 21, 1903.

39. Geelmuyden, Zeitschr. f. physiologische Chemie. Bd. XXIII.

40. Rosenfeld, Centralblatt f. Innere Medicin. No. 51. 1895.

41. Hirschfeld, Zeitschr. f. Klinische Medicin. Bd. XXVIII and Bd. XXXI.

42. Kraus und Honigman, pathologie d. Autointoxicationen. Ergebnisse der Allg. Path. Morphologie u. Physiologie d. Menschen. Herausgeg. v. Lubarsch u. Ostertag, 1895.

43. Stern, Some observations on the relation of the alkalescence of the blood to the urinary reaction. N. Y. Med. Jour., Aug. 17, 1901.

44. Camerer, Ueber Gicht u. Rheumatismus. 23 Vers. d. Balneolog. Ges. Stuttgart, March, 1902.

45. Weisz, Ueber Gicht. Balneolog. Ges. Stuttgart, March, 1902.

46. Sajous, The internal secretions and the principles of medicine. 1903.

47. v. d. Bergh, Ueber die Giftigkeit des Harns. Zeitschrift f. Klin. Med. Bd. 35.

48. Ewald u. Jacobson, Ueber Tetanie. Congress f. Innere Medicin. 1893.

49. Albu, Ueber die Ausscheidung toxischer Substanzen aus dem Organismus. Berl. Klin. Wochenschr. 1894. No. 48.

50. Ewald, Discussion—Autointoxicationen Intestinalen Ursprungs. Congress f. Innere Medicin. 1898.

.51. Senator, Die Erkrankungen der Nieren. Nothnagel's Specielle Pathologie und Therapie. XIX.

52. Strauss, Die chronischen Nieren-Entzuendungen in ihrer Einwirkung auf die Blutfluessigkeit und deren Behandlung, Berlin, 1902.

53. v. Korányi, Berliner klin. Wochenschr., 1899, No. 36.

54. Stern, A contribution to the pathogenesis of the uraemic state; the probability of its physico-electric substratum. Med. Rec., Jan. 24, 1903.

55. Lindemann, Die Concentration de Harns und Blutes bei Nierenkrankheiten etc. Deutsches Archiv f. klin. Med. LXV.

56. Stern, Jour. Am. Med. Ass. July 27, 1901.

57. Novi, Lo Sperimentale, 1857.

58. Landois, Die Uraemie. Zweite Auflage, 1891.

59 Viola, Revista veneta di science Mediche, 1901.

60. Bugarski und Tangl, Ueber die molekulare Concentration des Blutserums. Pflueger's Archiv, 72. 1898.

61. Bunge, Lehrbuch der physiologischen und pathologischen Chemie. 1898.

62. Stern, Constitution and Biology of Brewers' Yeast. Med. Rev. of Rev., April, 1904.

63. Starling, Jour. of Phys., XVII., 1894.

64. Magnan, Rescherches sur les Centres Nerveux, Paris, 1876.

65. Stern, Epilepsia alkoholica, Medical News, Sept. 18, 1897.

66. Moreigne, Arch. de Méd. experiment, 1899.

67. Stern, concerning the suppression of the acetone bodies in diabetes, American Medicine, Dec. 3, 1904.

68. v. Noorden, Berl. klin. Wochenschr. 1903.

69. Mossé, Mémoires communiqués a l'Académie de médicine, 1901, 1902.

70. Schwarz, Deutsches Arch. f. Klin. Med. Bd. 76, 1903.

71. Mueller and Masuyama, Zeitschr. f. Biologie Bd. 39.

72. Obesersky, Medizina, Nos. 47 and 48, 1899.

73. Stern, Coma diabeticum: its treatment. Jour. Am. Med. Ass. Dec. 8, 1900.

74. Stern, A hitherto undescribed reaction following the inoculation of vaccine virus, American Medicine, May, 1901.

75. Kirnberger, Zur Therapie der Basedow'schen Krankheit. Therapie der Gegenwart, October, 1903.

76. Moebius, Muench, Med. Wochenschr, 4, 1903.

77. Burghart und Blumenthal Ueber die spec. Behandlung des Morbus Basedowii.—Therapie der Gegenwart, August, 1903.

78. Stern, On the Treatment of Obesity, Jour. Am. Med. Ass'n, Feb. 15, 1902. Also The Obesity of Adolescence, N. Y. Med. Jour., March 29, 1902.

79. Bedart et Mabille, Compt. rend. de la Societe biol. 50, p. 556-557.

80. Stern, Adonidin: Physiologic and Medicinal Properties. Merck's Archives, April and May, 1900.

81. Stern, on the Relation of Obesity to Improcreance, Am. Med., Dec. 20, 1902.

82. Boinet, Compt. rend. de la Société biol., 51, p. 891.

83. Stern, Some Points Pertaining to the Therapeutic Management of the Uremic State. Transactions Med. Soc. State of New York, 1903, also in Am. Med., May 2, 1903.

84. Roberts, Urinary and Renal Diseases, 4th Ed. Phila., 1885.

INDEX

ABSINTHE, 132.
Acetone, 23, 60, 61, 62, 63, 68 86, 132.
Acetone bodies, fat mother substance of, 68, 151.
Acetone bodies (see also acetone, acid diacetic and acid beta-oxybutyric), 68, 145, 151, 152, 164, 165.
Acetone bodies, suppression of, 153.
Acetonemia, 63.
Acetonuria, intestinal, 60, 71, 145, 146.
Acetonuria, intestinal treatment of, 145.
Acetonuria, non-diabetic, treatment of, 164.
Acetonuria, of pregnancy, 164.
Acid, acetic, 22, 33.
Acid, beta-oxybutyric, 68, 69, 70, 86.
Acid butyric, 22, 155.
Acid caproic, 23.
Acid caproic, 155.
Acid carbonic, 64.
Acid cholic, 33.
Acid, chrysophanic, 35.
Acid coma, 669.
Acid, diacetic, 60, 61, 62, 63, 68, 132.
Acid, formic, 22, 122, 137.
Acid glycocholic, 78.
Acid, glycuronic, 33, 86.
Acid, hydrosulphuric, 22, 23.
Acid intoxication, cryptogenic (see also acidosis), 54, 69.
Acid, lactic, 22, 86.
Acid, oleic, 156.
Acidosis (see also acid intoxication), 66, 68, 69, 70, 71, 72.
Acidosis, catabolic, 150, 151, 152.
Acidosis, diabetic, 152.
Acidosis, diabetic, treatment of, 153, 156, 163.
Acidosis, intestinal (see also acetonuria, intestinal and diaceturia intestinal), 150, 151, 152.
Acidosis, sodium carbonate in, 72, 163.
Acidosis, treatment of, 150.
Acid palmitic, 155.
Acid, paraoxyphenylpropionic, 22.
Acid, phenylacetic, 22.
Acid, phenylpropionic, 22.
Acid, proprionic, 22.
Acid, rheumic, 35.
Acid, stearic, 156.
Acid, succinic, 22.
Acid, taurocholic, 78.
Acid, uric (tartronylcyanamid), 64, 73, 74, 75, 76, 89, 108.
Acid, valerianic, 22, 155.
Acid, sulphuric, 33.
Acne, 36, 41, 130.
Acromegaly, 77.
Acromegaly treatment of, 180.
Addison's disease, 76, 86, 179.
Addition, 32.
Adipolysis, 77.
Adipositas, pathologic, 76, 135.
Adonidin, 177.
Adrenals, 76, 77.
Adrenals, metabolizing function of, 179.
Aerophagia, 56.
Air baths, 130.
Albuminuria, 36, 37.
Alcoholism, 43.
Alimentary tract, disturbances of, 36.
Alkali contents, of body, 67.
Alkalies in acidosis, 162, 165.
Alkalies, salt action of, 171, 191.
Alkaloids, bacterial, 87.

Alloxuric bodies, 72.
Alopecia universalis, 41.
Aloes, 118.
Amido-acids, 23, 69.
Ammonemia, 85.
Ammonia, 22, 23, 67, 69, 89.
Ammonium carbonate, 85, 89.
Amyl nitrite, 138.
Anemia, 75.
Anemia, pernicious, 59, 68.
Angina pectoris, 56.
Antibodies, 29, 31, 32, 65.
Antiferment, 29, 30.
Antikinase, 29.
Antipeptic activity, 29, 30.
Antirennet, 29.
Antiseptics, 120.
Antitryptic activity, 29, 30.
Aperient mineral waters, 131, 170.
Apomorphine, 116.
Aromatic substances, 23.
Arsenic, 144, 177.
Asafetida, 142.
Asthma, 45.
Asthma dyspepticum, 55, 56.
Asthma dyspepticum, treatment of, 137.
Athyroidism, 175.
Atropin, 131, 137, 141, 142, 148, 181.
Autochthonus intoxication, 15, 16, 25.
Autodigestion, 30.
Autoinfection, 16, 18, 19, 20, 86.
Autointoxication, catabolic, 18, 20, 38, 64.
Autintoxication, intestinal, treatment of, 113, 126.
Autointoxication, intestinal, 18, 24, 31, 32, 34, 36, 37, 38, 42, 54, 69, 79.
Autointoxication, chronic, 39, 40, 56.
Autointoxications, therapy of, 111.
Autolysis, 65, 77, 149, 150.
Autoprotection, 31.
Autotoxicosis, histolytic, 65.
BACTERIA, intestinal, 23, 24, 38.
Bacterial poisons, 19.
Basedow's disease, 173.
Bile, 24, 78.
Biliousness, 78.
Bismuth salicylate, 141.
Blennosis, gastric, 56.
Blood alkali, 33.
Blood, alkalescence of, 71, 72.
Blood, hyperosmosis of, 90, 91, 92, 93, 95, 101.
Blood, isotony of, 84.
Blood, esmotic tension of, 90, 91, 104, 105.
Blood, sodium carbonate in, 67.
Bradycardia, 43.
Bromides, 137, 142, 201.
Bronchitis, 75.
CAFFEINE, 73.
Cachexia, carcinomatous, 68.
Cachexia, carcinomatous, 164.
Cachexia, pachydermic, 175.
Cachexia strumipriva, 175.
Cadaverin, 60.
Calcium carbonate in coma, diabetic, 163.
Calcium oxalate, 35.
Calomel, 43, 121, 131, 137, 142, 170.
Camphor, 142.
Camphor, monobromide, 142.
Carbamid (see also Urea), 64, 82, 83, 89, 98.
Carbon dioxide intoxication, treatment of, 147, 148.
Cascara sagrada, 118.
Castor oil, 118.
Casts, hyaline, 36.
Catabolic autintoxication, treatment of, 147.
Cerebro-spinal fluid, 43.
Chills, 36.

Chloral hydrate, 137, 142, 201.
Chlorids, in the blood, 104, 105.
Chlorids, urinary, 103, 104.
Chloroform, 141, 142, 200.
Chlorosis, 58.
Chlorosis, treatment of, 142.
Cholagogues, 118.
Cholemia, 77, 78.
Cholemia, treatment of, 182.
Cholera, 18.
Cholerestin, 97.
Cholin, 43.
Chorea, 75.
Circulation, 31, 32.
Cocain, 137.
Colchicum, 168.
Colocynth, 118.
Coma, carcinomatous, 164.
Coma, cholemic, 183.
Coma, dyspneic (see also coma and acidosis), 63, 97, 109, 152, 163.
Coma, dyspheic (see also coma, diabetic), 152.
Complement, 28.
Convulsions, infantile, 58.
Copper sulphate, 116.
Coprostasis, 142.
Creatin, 89.
Creatinine, 89.
Creosote, 141.
Cresol, 22.
Cretinism, 175.
Cystein, 33.
Cystinuria, 59, 60.
Cystinuria, treatment of, 144.
DECOMPOSITION products, 20.
Dehydration, 32.
Dehydration (of the organism), 57.
Dermatitis exfoliativa, 41.
Dermatoses, 40.
Dermatoses, antidotal treatment of, 129.
Diabetes melitus, 43, 68, 75, 109, 129, 135, 183, 184, 187.
Diacetemia, 63.
Diaceturia, intestinal, treatment, 71, 145, 146.
Diaceturia, intestinal, treatment of, 145.
Diaminuria, 59, 86.
Diaminuria, treatment of, 144.
Diaphoretics, 126, 192, 193.
Diathesis, uric acid, 74.
Dihydrogen sulphate, 67.
Diphtheria, 18.
Disorders, nervous and mental, 36, 42.
Dissociation, 95, 96, 100.
Distilled water, toxicity of, 81.
Diuresis, 126.
Drastics, oily, 117.
Drug narcotization, 43.
Dyscracy, 34.
Dyspnea, 36.
ECLAMPSIA, albuminuria in, 204.
Eclampsia, of pregnancy, 164.
Eclampsia, infantile, 58.
Eclampsia, liver as etiological factor of, 202.
Eczema chronicum, 41, 42.
Elimination, faulty, 34.
Emetics, 116.
Emunctories, vicariousness of, 90.
Endogenous intoxication, 19.
Enema, 118, 119.
Enteric fever, 18, 43.
Enteritis, 56.
Enteroclysis, 118, 119, 120, 126.
Enterokinase, 26, 28, 29.
Enteroproducts, 129.
Entero-toxicosis, 22, 34.
Enterotoxin, 115, 126, 129, 173.
Enzyme, amylolytic, 26.
Epilepsia alkoholica, 132.

Epilepsy, 42, 75.
Epilepsy, treatment of, 132.
Epileptiform disorders, treatment of, 132, 133.
Equation, toxic and autotoxic, 35.
Erepsin, 26.
Erysipelas, 87.
Erythema, 34, 36, 41, 130.
Ether, 201.
Ethereal sulphates, 23.
Eucalyptus, 138, 143.
Excretory organs, insufficiency of, 41.
Exercise, 130, 138.

FATS, absorption of, 25.
Fats, splitting of, 25.
Fatty acids, 25, 64, 115, 145, 155.
Ferment, modified, 30.
Fermentation, 22, 23, 29.
Ferric chlorid reaction, 61.
GARLIC, 142.
Gas interchanges, respiratory, 64.
Gastrectasia, 56.
Gastrectasia, treatment of, 140.
Gastric irrigation, 115.
Gastric lavage, 115, 116.
Gastroenteritis, 43.
Gastro-intestinal canal, evacuation of, 115.
Gastro-intestinal poisons, neutralization of, 120, 121.
Gland, metabolizing function of (see also secretion, internal), 172, 173, 178.
Glucose, 41, 130.
Glycocol, 33.
Glycocyamidin, 87.
Glycolytic function, augmentation of, 130.
Glycoproteids, 27.
Goiter, exophthalmic, 173.
Gout, 73, 74.
Graves' disease, 76.
Graves' disease, treatment of, 173, 174.
HAEMATOPORPHYRINURIA, 183, 185.
Hay fever, 75.
Helminthiasis, 56, 58, 139.
Hemoglobinuria, 75.
Histolytic autotoxicoses, treatment of, 149.
Histoenzymic Autotoxicoses, treatment of, 171.
Histolytic autotoxicoses treatment of, 149.
Hot air therapy, 130.
Hydration, 32.
Hydrogen sulphide, 33.
Hydrolysis, 65.
Hydrotherapy, 134.
Hydrothionemia, 38.
Hyperchlorhydria, 104.
Hyperglycemia, 41, 129
Hyperthroidism, 173.
Hypodermoclysis, 125, 126, 197.
Hysteria, 75.
ICHTHYOSIS, 41, 65.
Icterus, 36, 37.
Icterus non-gravis, 183.
Idiosyncrasy, 34, 35.
Impermeability, renal, 41.
Impetigo, 130.
Indol, 22, 83.
Indoxyl-potassium sulphate, 53.
Infantile convulsions, treatment of, 141.
Infection, 18, 37.
Infection-autointoxication, 19.
Infectious diseases, acute, 43, 87.
Influenza, 43, 87.
Infusion, intravenous, 125, 126, 197.
Intestinal autotoxicosis, etiological treatment of, 114, 115.

Intoxication, intestinal, treatment of, 113.
Intrabiontic intestinal poisons, 20, 31.
Iodin, 168, 173.
Iodism, 35.
Ions, friction in uremic serum, 95.
JODIDS, 35.
KERATODERMITES, 41.
LEAD poisoning, acute, 122.
Lecithin, 43, 97.
Leucemia, 59, 68, 74, 164.
Leucemia, treatment of, 143.
Leucin, 23, 64, 89.
Leucomains, 87.
Lichen, 41.
Linderae cortex, 193.
Liquor thyroidei, 176.
Lithemic state, 74.
Lithium, 170.
Liver, 31, 32.
Liver, acute yellow atrophy of, 182.
Lung gymnastics, 130, 138.
Lupulin, 141.
Lymph, metabolism of, 124, 135.
Lymph metabolism, stimulation of, 124.
Lymphagogue, 124, 125, 126.
MAGNESIA usta, 141.
Magnesium citrate, 117.
Malaria, 135.
Measles, 87.
Meningoform disturbances, 42, 131.
Methylendiamin, penta and tetra, 59.
Methylmercaptan, 22.
Microorganisms, pathogenic, 18, 20.
Milk, of thyroidectomized goats, 174.
Milk-fat, exclusion from diet, 142.
Molecular concentration, intrabiontic, 58.
Molecules, organic, 89, 90, 98.
Morbid sleepiness, treatment of, 134.
Morphin, 137, 199.
Mucin, 27.
Mucosa, intestinal, 25, 26, 27, 29, 31.
Mucus, intestinal, 27.
Mustard, pulverized, 116.
Myasthenia gravis pseudoparalytica, 42.
Myxedema, 76.
Myxedema, treatment of, 175.
NARCOLEPSY (see also sleepiness and somnolence, pathologic, 43, 44, 103.
Narcolepsy, treatment of, 134.
Nephritis, 74, 75, 91, 93.
Nephritis, chronic interstitial, 35, 99.
Nephritis, chronic parenchymatous, 35, 99.
Nephritis, treatment of preuremic stages, 191.
Neptune's girdle, 137.
Neuralgia, 42.
Neurasthenia, 75, 131.
Neuroses, 42.
Neuroses, treatment of, 131.
Nitrogen, retained, 94, 95, 99, 101, 189, 190, 198.
Nitroglycerin, 138, 142.
Nosotoxicoses, 19.
Nucleins of food, 73.
Nucleolytic autotoxicoses, treatment of, 166.
Nucleolysis, 72.
Nucleolysis, catabolic, 76, 77, 166, 167, 168.
OATMEAL cure, 153.
Obesity, pathological, treatment of, 177.
Obstipation, 43.
Oliguria, 36, 37.

Oophorin, 179.
Organo-therapy, 171.
Osmotic equilibrium, disturbance of, 57.
Ovarian grafting, 178.
Ovarian substance, administration of, 178.
Ovaries, 76, 177, 178.
Ovulation, 177.
Oxidation, 32.
Oxy-acids, 69.
Oxygen, treatment by, 148.

PANCREAS, 28, 76.
Pan, disease of, 55.
Paralysis, acute ascending, 42, 131.
Paralysis, periodic, 42.
Parathyroid, 76.
Parathyroid function, 173.
Pemphigus, 41, 130.
Periodical vomiting, treatment of, 137.
Pernicious anemia, treatment of, 143.
Pertussis, 87.
Phenol, 22.
Phenol, 141.
Phthisis pulmonum, 35.
Physical autointoxication, 85, 88, 90, 108.
Physico-electric equilibrium, 67.
Pigmentary substances, 89.
Pilocarpin, 193.
Pituitary body, 76.
Pituitary body, disturbance of activity of, 180.
Pituitary body, extract of, 180.
Plasmolysis, 77.
Pleuricin, 87.
Pleurisy, urine in, 87.
Pneumonia, urine in, 87.
Polysarcia, 43, 135.
Polysarcia after oophorectomy, 177.
Potassium and sodium tartrate 117, 170.
Potassium bitartrate, 117.
Potassium poisoning, 89.
Potassium tartrate, 117.
Potatoe cure, 154.
Protectors, chemical, 32.
Protective reaction, 32.
Proteolysis, 29.
Protoplasm, destruction of, 65.
Prorigo, 41.
Psoriasis, 41, 65.
Psychoses, acute, 53.
Psychoses, treatment of, 135.
Ptomains, in urine, 86, 87.
Puerperal Eclampsia, treatment of, 201.
Purgatives, oily, 117.
Purins, 72, 166, 167, 170.
Putrefaction, 22, 23, 29
Putrescin, 60.

RAYNAUD'S disease, 75.
Reduction, 32.
Resorcin, 141.
Retention autotoxicoses, treatment of, 147.
Retention-histolytic autotoxicoses, combined, 77.
Rheum, 35.
Rheumatism, 75.

SALINE purgative, 117, 170.
Salivary glands, 76.
Salt solution, decinormal, 198.
Salt solution, hypotonic, 198.
Salt solution physiologic, 197.
Scorbut, 68.
Secretion, external, 172.
Secretion, intestinal, 26, 27.
Secretion, internal, 76, 77, 172, 175.
Secretion, internal (see also metabolizing function of gland), 66.
Serotoxicity, 95.
Serum, artificial, infusion of, 99.

Serum, electrical conductivity of, 57, 96, 97, 98, 99, 100, 109.
Serum, freezing-point of, 91, 93.
Serum, intravenous injection of, 81.
Serum, molecular concentration of, 90, 91, 93, 96, 101.
Serum, mitrogenous molecule in, 95.
Serum, non-electrolytes in, 95, 97, 101.
Serum, of thyroidectomized animals, 174.
Sexual glands, atrophy of, 178.
Sialagogue, 127.
Skatol, 22, 83.
Skin, burns and scalds of, 65.
Skin, respiratory function, 64.
Sleepiness, morbid (see also somnolence, pathologic, and narcolepsy), 85, 100.
Snake venom, 115.
Sodium chloride, 124, 125, 126, 135.
Sodium formate, 122.
Sodium Glycocholate, 78.
Sodium phosphate, 117, 170.
Sodium pyrophosphate, 117, 170.
Sodium sulphanilate, 173.
Sodium sulphate, 117, 170.
Sodium sulphide, 122, 130, 137, 142.
Sodium tartrate, 117.
Sodium tanrocholate, 78.
Solvents, physiological, 166, 168, 169.
Somnolence, pathologic, 43, 46, 70, 103, 105.
Spermin, 179.
Spiritus glonoin, 138.
Spleen, excretory function of, 76.
Stern's trocar, 195, 196, 197.
Strychnin camphoricum, 163.
Sulphonal, 184, 186.
Sulphur-mud baths, 171.
Supra-renal capsules, 76, 77.
Supra-renal extract, 179.
Sweat secretion, stimulation of, 126.
Sympathectomy, 173.
TEMPERATURE, influence upon electric conductivity of serum, 100.
Testicular substance, 179.
Tetanus, 18.
Tetany, 56, 86.
Tetany, artificial, 57.
Tetany, treatment of, 138.
Tetronal, 184, 186.
Thoracic duct, lymph-flow from, 125.
Thymol, 141.
Thymus ingestion, 74.
Thymus secretion, 76.
Thyroid, 173, 175.
Thyroid, powdered gland, 176.
Thyroid feeding, 176.
Thyroid gland, excretion of, 76.
Thyroidectomy, 173.
Toxemia, 32, 35.
Toxicity, relative urinary, 49, 52, 85.
Toxicuria, 87.
Trional, 184, 186.
Trymethyl-Xanthin, 73.
Trypsin, 28, 29.
Trypsinogen, 28.
Tuberculosis, 18.
Typhus, 43.
Tyrosin, 23, 64.
ULCER, duodenal, 30.
Ulcer, follicular, 30.
Ulcer, perforating gastric, 30, 56.
Urea (see also carbamid), 33, 64.
Uremia, 77.
Uremia, catharsis in, 191.
Uremia, chloroform in, 200.

Uremia, coma of, 109.
Uremia, cutaneous manifestations in, 41.
Uremia, diaphoresis in, 192.
Uremia, freezing-point of serum in, 94.
Uremia, hypodermoclysis and infusion in, 197.
Uremia, morphin in, 199, 200.
Uremia, pathogenesis of, 88.
Uremia, serum of, in chronic interstitial nephritis, 189, 190.
Uremia, serum of, in chronic parenchymatous nephritis, 189, 190.
Uremia, treatment of, 188.
Uremia, venepuncture in, 195.
Uremia, venesection in, 193.
Uremic serum, neutral molecules in, 95, 96.
Uricacidemia, 74.
Urinary toxicity, 81, 82, 83, 84, 85.
Uric acid solvents, physiologic, 74, 75.
Urine, alkalinization of, 71.
Urine, autotoxic factors in, 81.
Urine, biological analysis of, 84, 85.
Urine, decolorization of, 85.
Urine, molecular concentration of, 84, 92.
Urine, scarlatinal, 87.
Urochrom, 89.
Urotoxic coefficient, 82, 84.
Urotoxy, 82.
Urticaria, 34, 36, 37, 41, 130.
Vaccine virus, influence upon catabolic nucleolysis, 168.
VENEPUNCTURE, 125, 195.
Venepuncture trocar, 125, 195, 196, 197.
Venesection, 125, 193.
Vertigo, gastric, 37.
Vicarious activity of emunctories, stimulation of, 149.
Vitiligo, 41.
Vomiting, periodical, 54, 55.
WATER, infusion of, 99.
XANTHIN bases, 73, 166, 167, 170.
YEAST, brewer's, 122, 123, 130, 142.
Yeast, dried, 122, 130, 142.
Yolk, composition of, 157.
Yolk cure, 156, 158, 159, 165.
Yolk cure, technic of, 159, 160.
Yolk, diastatic ferment in, 157.
Yolk dishes, 160, 161.
Yolk, lecithin contents, 157.
Yolk menu, 160.
Yolks, as food, 142, 145.
ZINC sulphate, 116.
Zymase, 122.